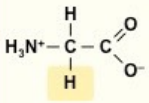
Amino Acids and Protein Structure

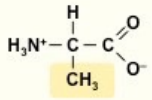
Damian Pajor

AA SIDE CHAINS

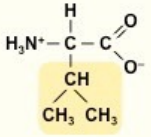
NON-POLAR



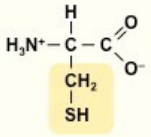
Glycine
(Gly / G)



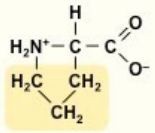
Alanine
(Ala / A)



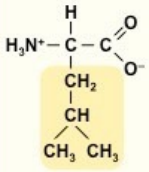
Valine
(Val / V)



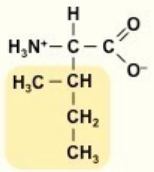
Cysteine
(Cys / C)



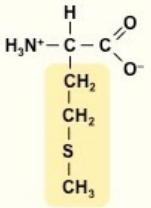
Proline
(Pro / P)



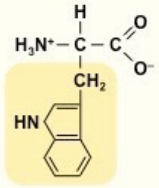
Leucine
(Leu / L)



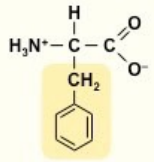
Isoleucine
(Ile / I)



Methionine
(Met / M)

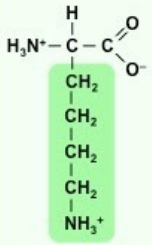


Tryptophan
(Trp / W)

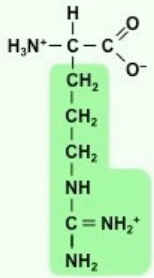


Phenylalanine
(Phe / F)

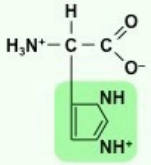
+ CHARGE



Lysine
(Lys / K)

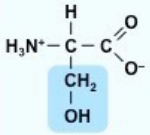


Arginine
(Arg / R)

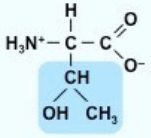


Histidine
(His / H)

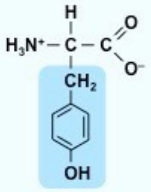
POLAR



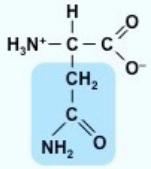
Serine
(Ser / S)



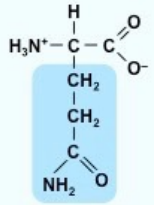
Threonine
(Thr / T)



Tyrosine
(Tyr / Y)

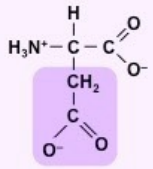


Asparagine
(Asn / N)

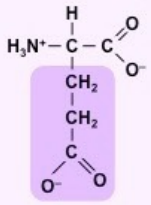


Glutamine
(Gln / Q)

– CHARGE

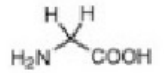


Aspartic Acid
(Asp / D)

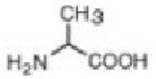


Glutamic Acid
(Glu / E)

Small

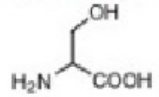


Glycine (Gly, G)
MW: 57.05

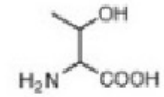


Alanine (Ala, A)
MW: 71.09

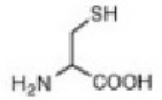
Nucleophilic



Serine (Ser, S)
MW: 87.08, pK_a ~ 16

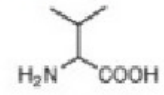


Threonine (Thr, T)
MW: 101.11, pK_a ~ 16

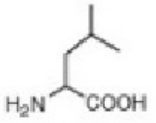


Cysteine (Cys, C)
MW: 103.15, pK_a = 8.35

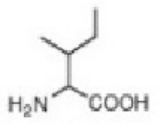
Hydrophobic



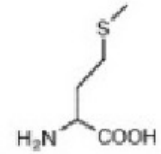
Valine (Val, V)
MW: 99.14



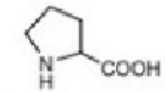
Leucine (Leu, L)
MW: 113.16



Isoleucine (Ile, I)
MW: 113.16

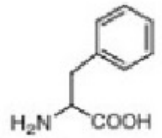


Methionine (Met, M)
MW: 131.19

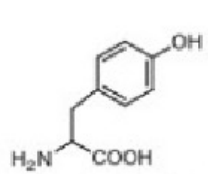


Proline (Pro, P)
MW: 97.12

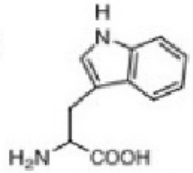
Aromatic



Phenylalanine (Phe, F)
MW: 147.18

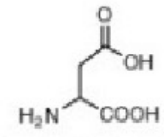


Tyrosine (Tyr, Y)
MW: 163.18

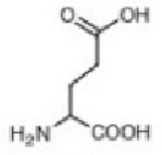


Tryptophan (Trp, W)
MW: 186.21

Acidic

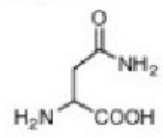


Aspartic Acid (Asp, D)
MW: 115.09, pK_a = 3.9

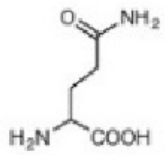


Glutamic Acid (Glu, E)
MW: 129.12, pK_a = 4.07

Amide

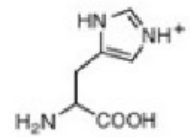


Asparagine (Asn, N)
MW: 114.11

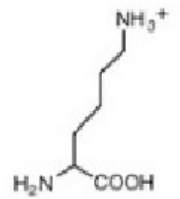


Glutamine (Gln, Q)
MW: 128.14

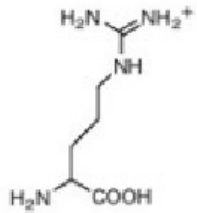
Basic



Histidine (His, H)
MW: 137.14, pK_a = 6.04



Lysine (Lys, K)
MW: 128.17, pK_a = 10.79



Arginine (Arg, R)
MW: 156.19, pK_a = 12.48

1 or 2

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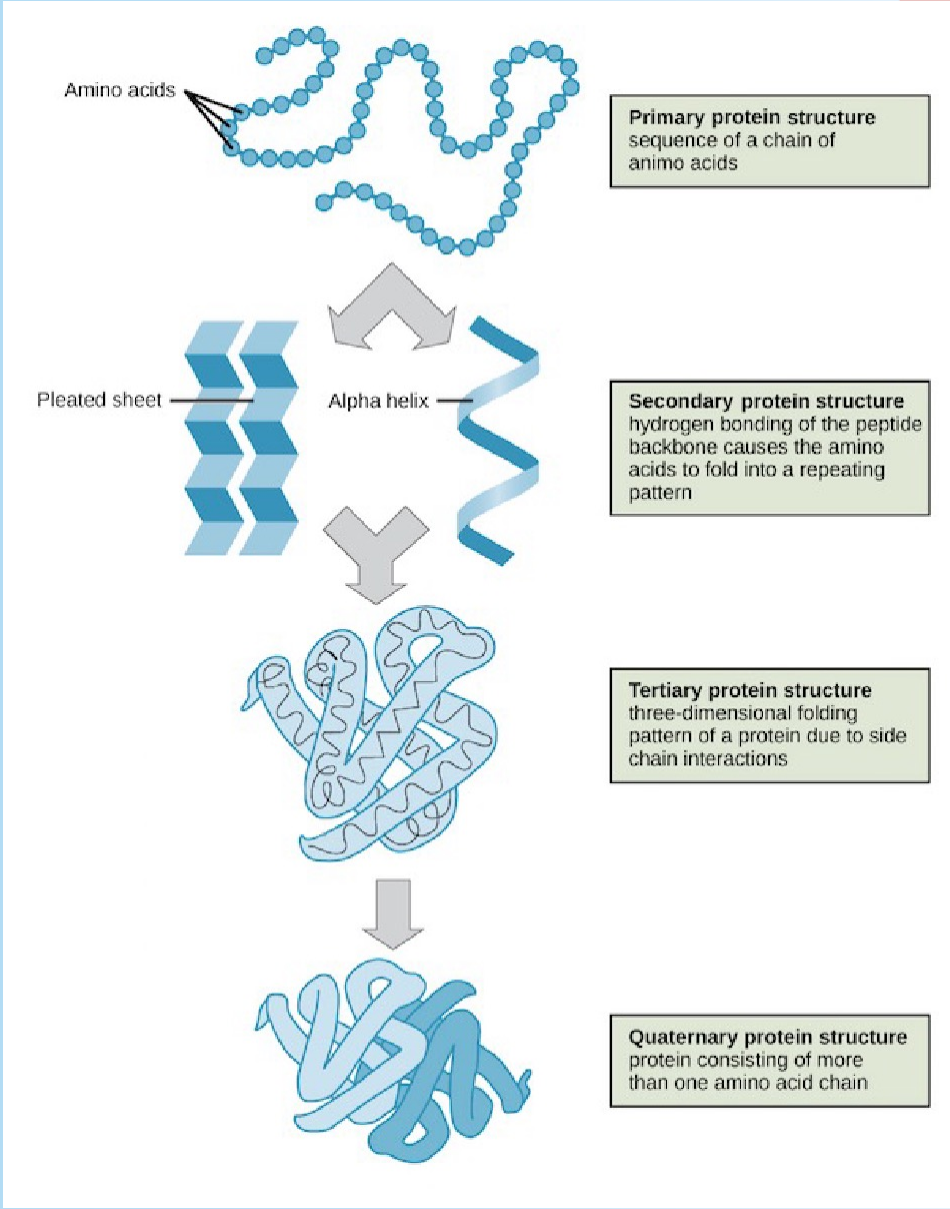
Overview

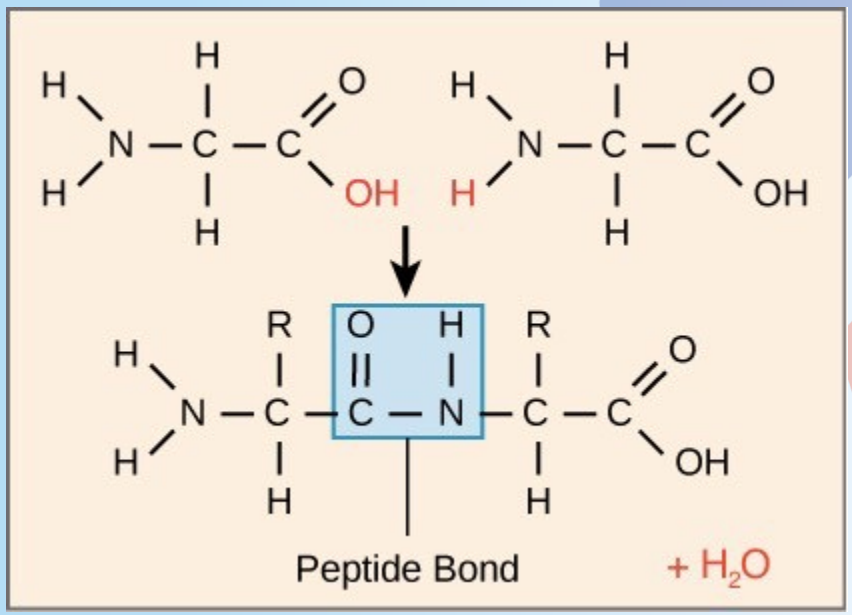
- Primary - the sequence of amino acids
- Secondary - alpha helix and beta sheets
- Tertiary – folding of alpha helix and beta sheets
- Quaternary – combination of 2 or more tertiary proteins to form multimers



Primary Structure

- The primary structure = sequence of amino acids in the polypeptide chain.
- The two ends
  - Amino terminus (N-terminus)
  - Carboxyl terminus (C-terminus)
  - The sequence is read from N→C

Condensation Reaction

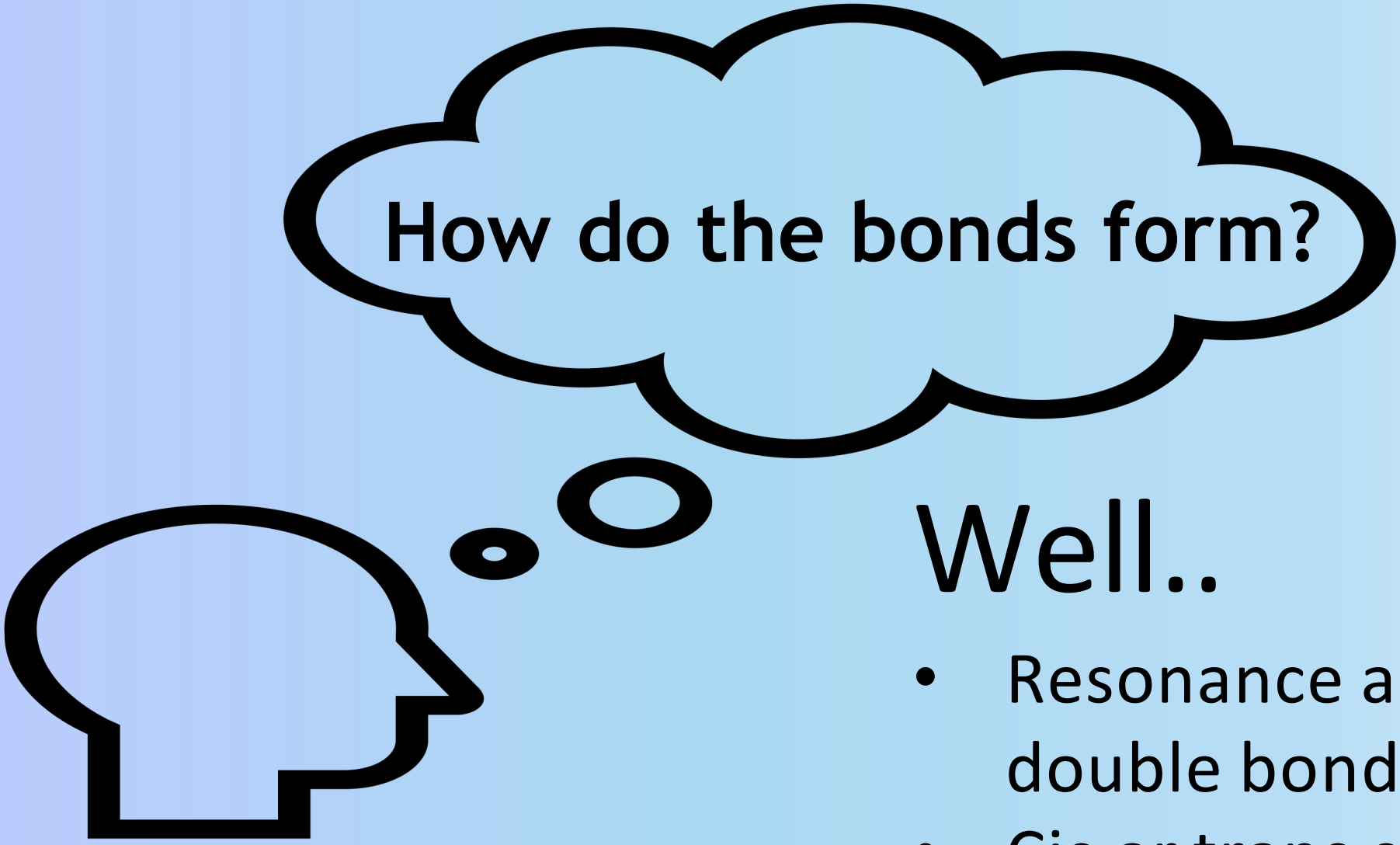


- Determined by the gene corresponding to the protein

- It is this sequence that determines the how it will fold
- **All of the info** about folding is in the primary sequence

Bonds

Peptide bonds – between C and N terminus of sequential AA

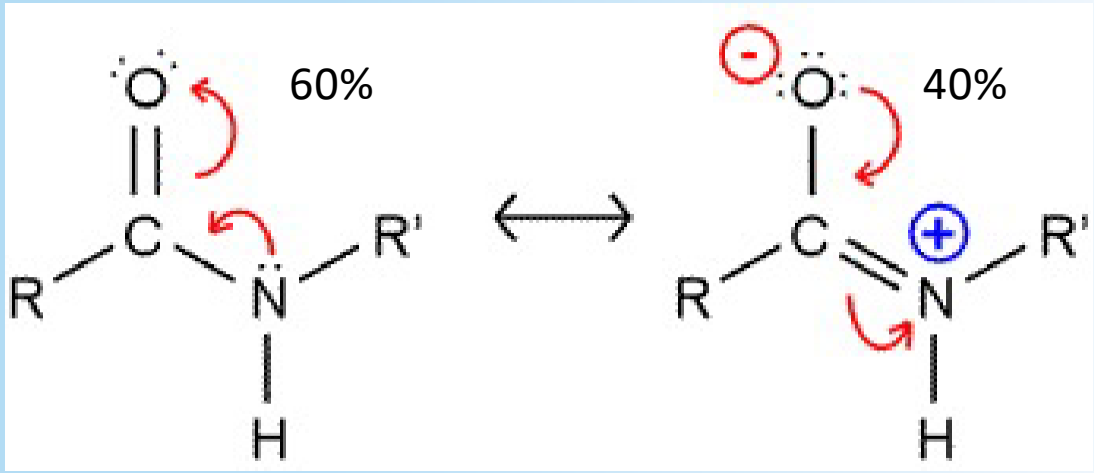


Well..

- Resonance and partial double bonds
- Cis or trans configuration
- Rotations

Partial Double Bonds

- sharing of electrons between bonds
  - single bonds between two atoms are longer than double bonds between the same two atoms
  - Ex. C-----N and/or C=N
  - The double bond resonance form of the peptide bond **helps to increase stability and decrease rotation around that bond.**

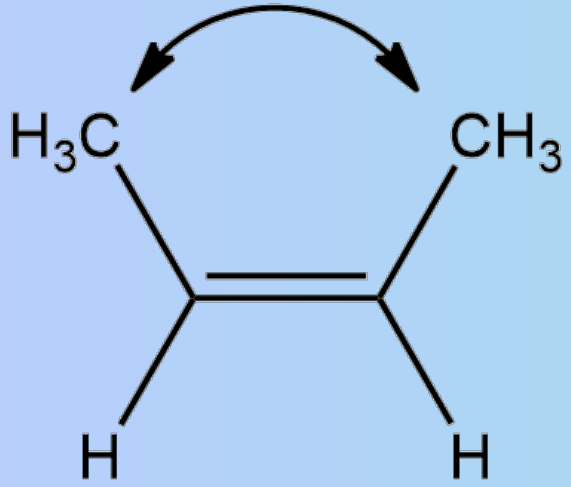


- During peptide bond formation the double bond moves from C=O to the C=N.

- The stability of the peptide bond is due to the resonance of amides. Nitrogen is able to donate its lone pair of electrons to the carbonyl carbon and push electrons from the carbonyl double bond towards the oxygen, forming the oxygen anion.

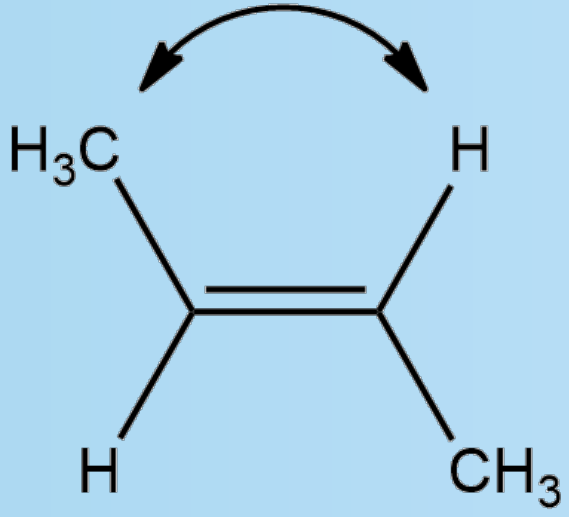
Cis and trans configuration

greater steric repulsion

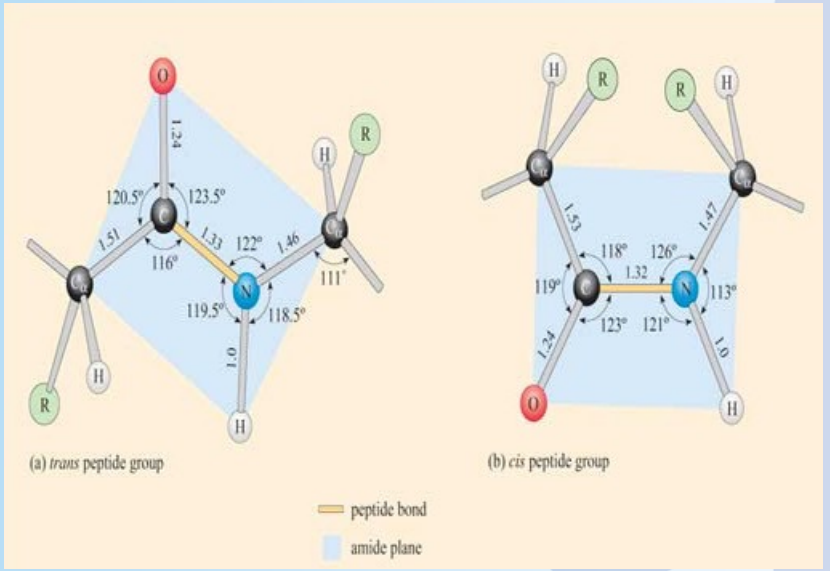


***cis* isomer**

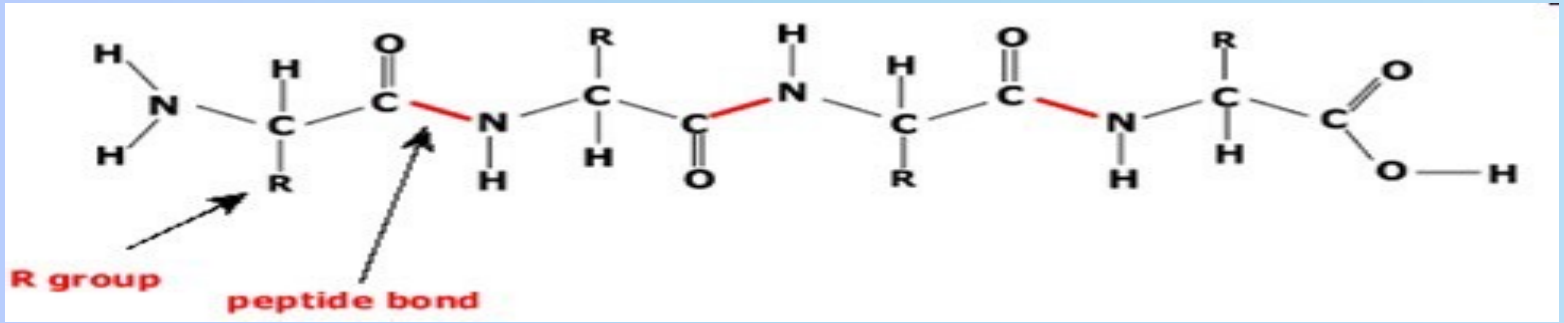
less steric repulsion

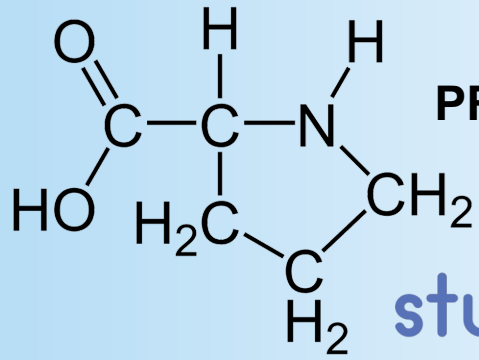


***trans* isomer**



Peptide bonds are in the *trans* conformation.
However, *cis* forms can occur in peptide bonds that precede a proline residue





PROLINE

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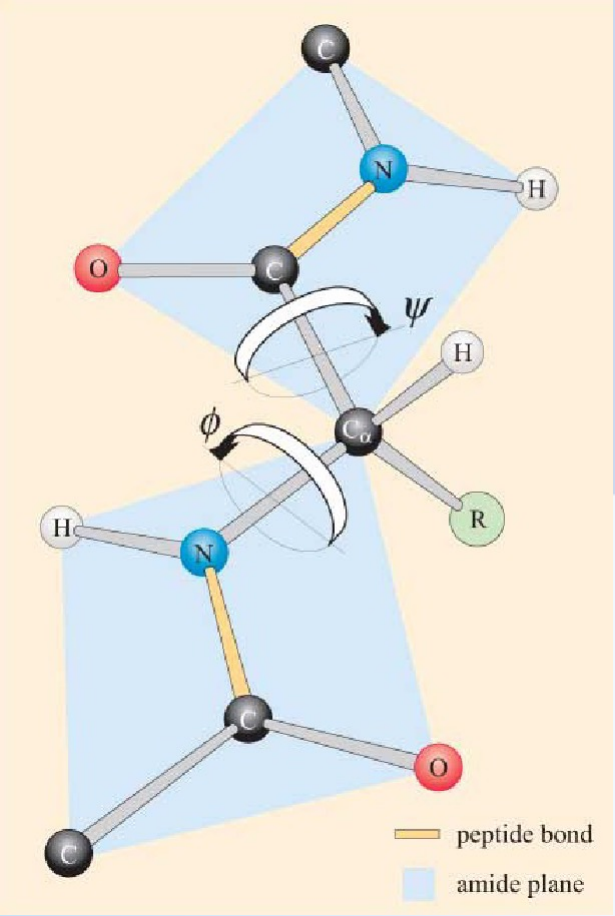
Steric Hinderance and Rotation

- **Steric hindrance** is when the large size of groups within a molecule prevents chemical reactions which can take place in related molecules with smaller groups.
- **Steric** meaning: in 3 dimensions
- **Hinderance** meaning: to prevent



- There is no rotation about the partially double peptide bond!
  - makes the peptide unit rigid and planar
- Where can rotation occur?
  - only around the bonds connected to the alpha carbons
  - Alpha C → C
  - Alpha C → N
- This is also a form of steric hinderance

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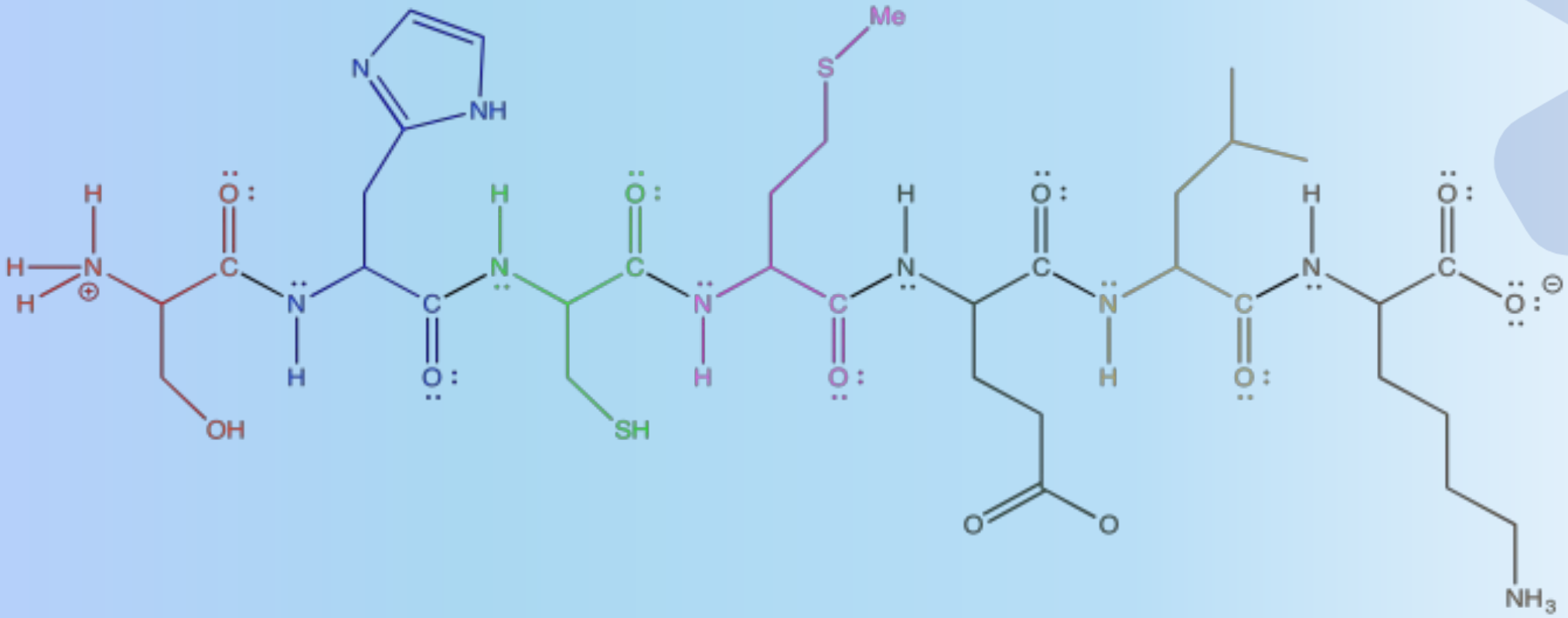
Rigid planar structure!



1	2	3	4	5	6	7
serine	histidine	cysteine	methionine	glutamic acid	leucine	lysine
Ser1	His2	Cys3	Met4	Glu5	Leu6	Lys7

Secondary structure

- The main types of secondary structure:
  - the α-helix
  - β-strand or β-sheets
  - B-turns
- defined by patterns of hydrogen bonds between the main-chain peptide groups.
- Both the α-helix and the β-sheet represent a way of saturating all the hydrogen bond donors and acceptors in the peptide backbone.

HYDROGEN BONDS

- H----F
- H----O
- H----N

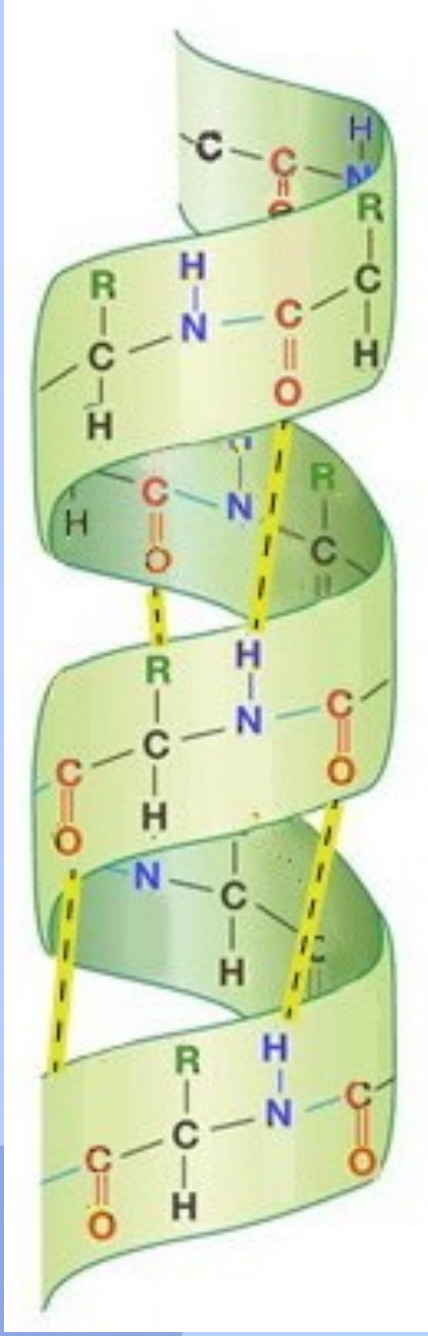
MAIN BONDS

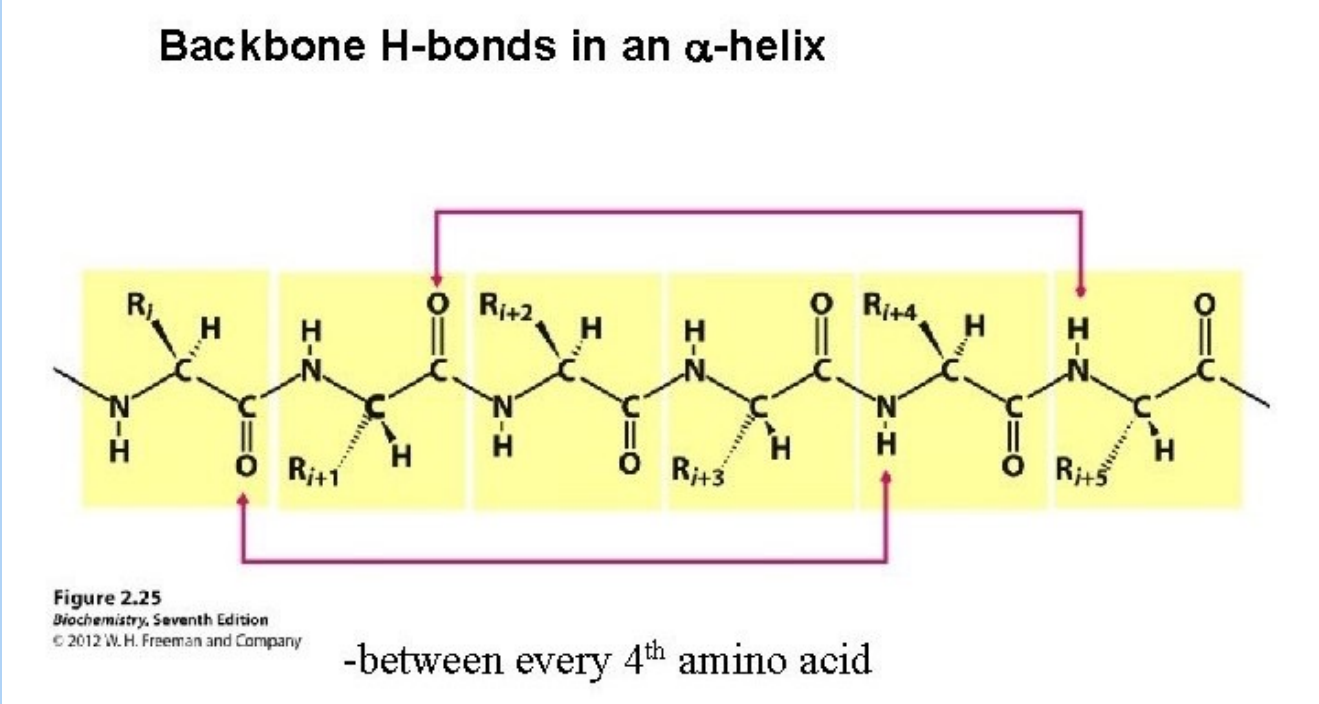
- C=O----H-N

REMINDER OF PEPTIDE BONDS

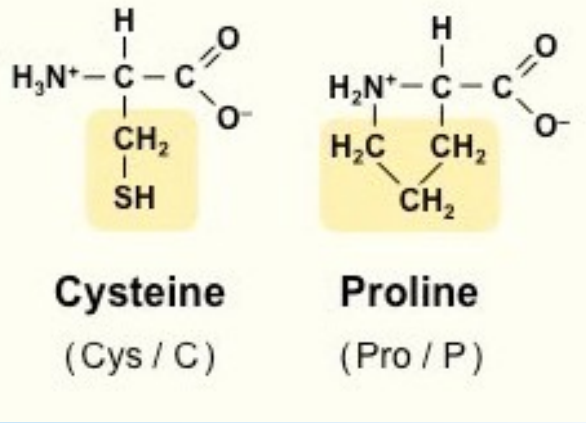
- O=C----N-H

Alpha helix





Look at the difference of proline as compared to other AAs.



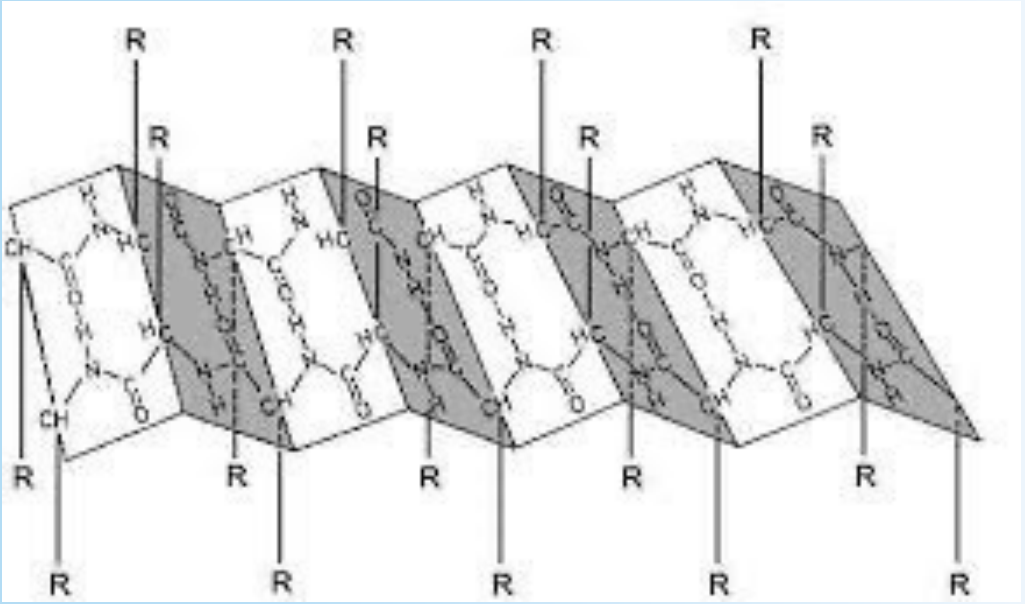
- Right handed helix! (Note the difference between alpha helix and collagen triple helix which is left handed!)
- 3.6 residues per turn
- Side chains project outward!
- Hydrogen bonds project parallel

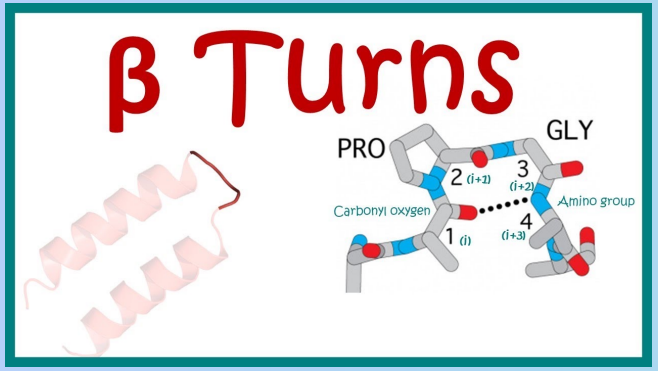
Proline is in a peptide bond, it does **not** have a hydrogen on the **α** amino group, so it cannot donate a hydrogen bond to stabilize an **α helix** or a β sheet.

studyaid

Beta-pleated sheets

- Composed of beta strands
- Sides chains project on both sides of the sheets (“over and under”)
- Hydrogen bonds project adjacent





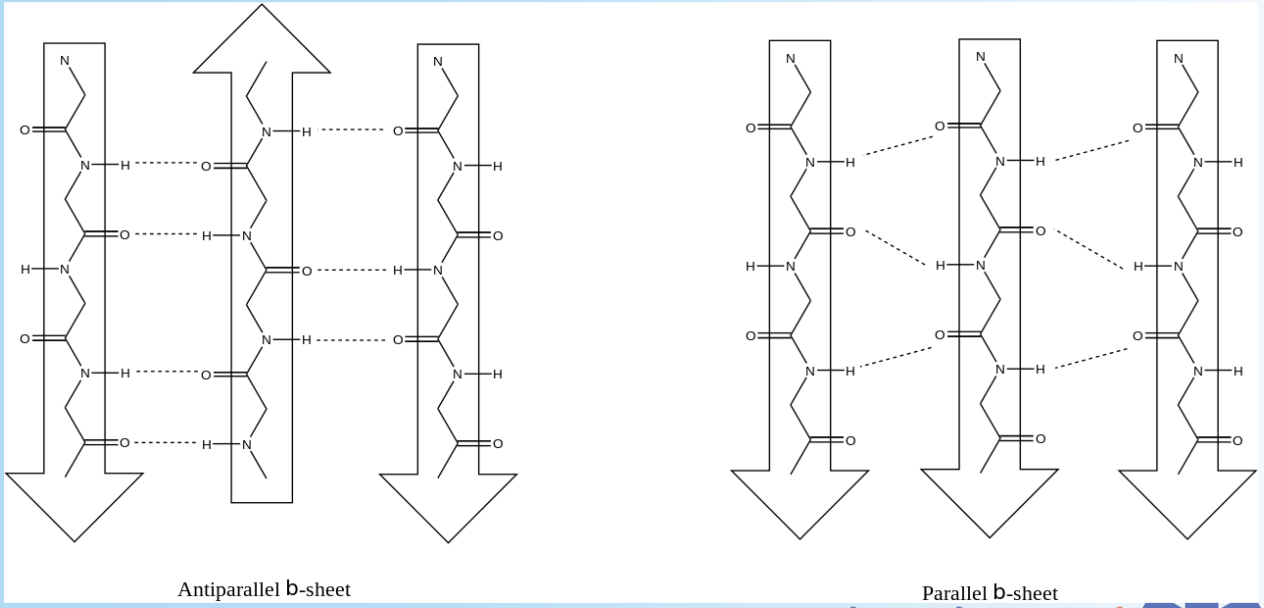
Turns and loops:

Connect adjacent beta strands

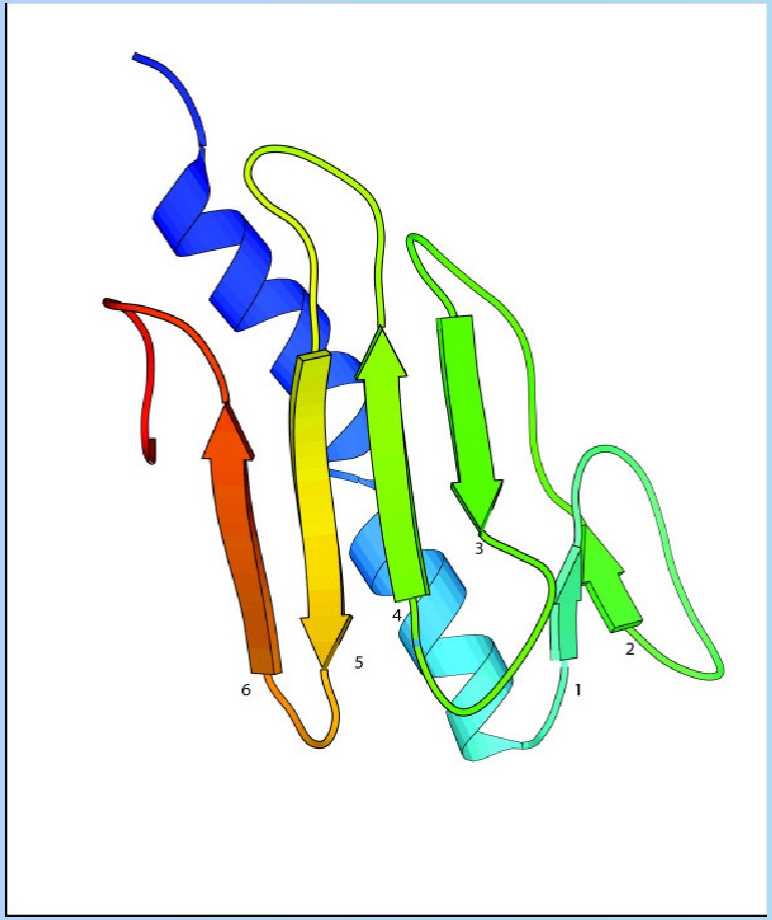
Beta turns: Connect adjacent ANTIPARALLEL beta strands

Contains a lot of:

- Proline (a turn needs that ”kink”)
- Glycine (has the smallest side chain→→ most flexible)

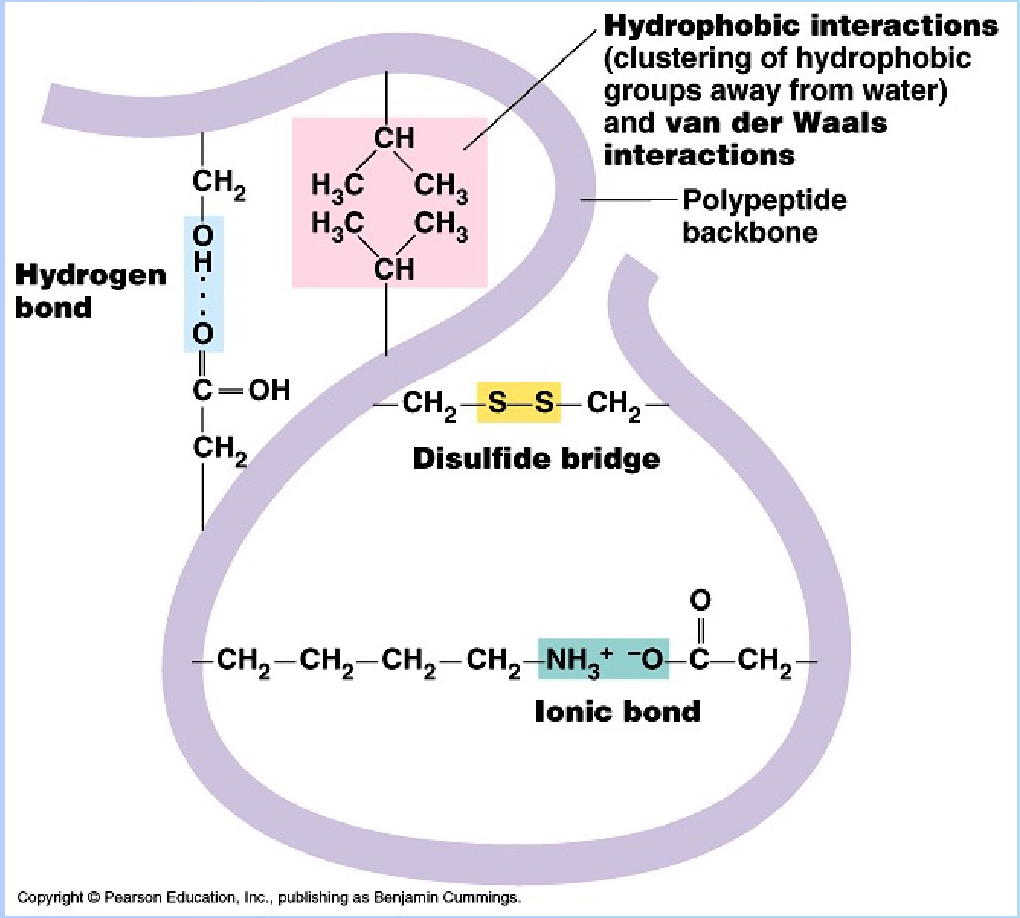


Tertiary structure



- the three-dimensional structure created by a single protein molecule (a single polypeptide chain).
- one or several domains
- The α-helixes and ß-pleated-sheets are folded into a compact globular structure.
- Globular proteins hydrophobic CENTER and hydrophilic “SHELL”

Bonds



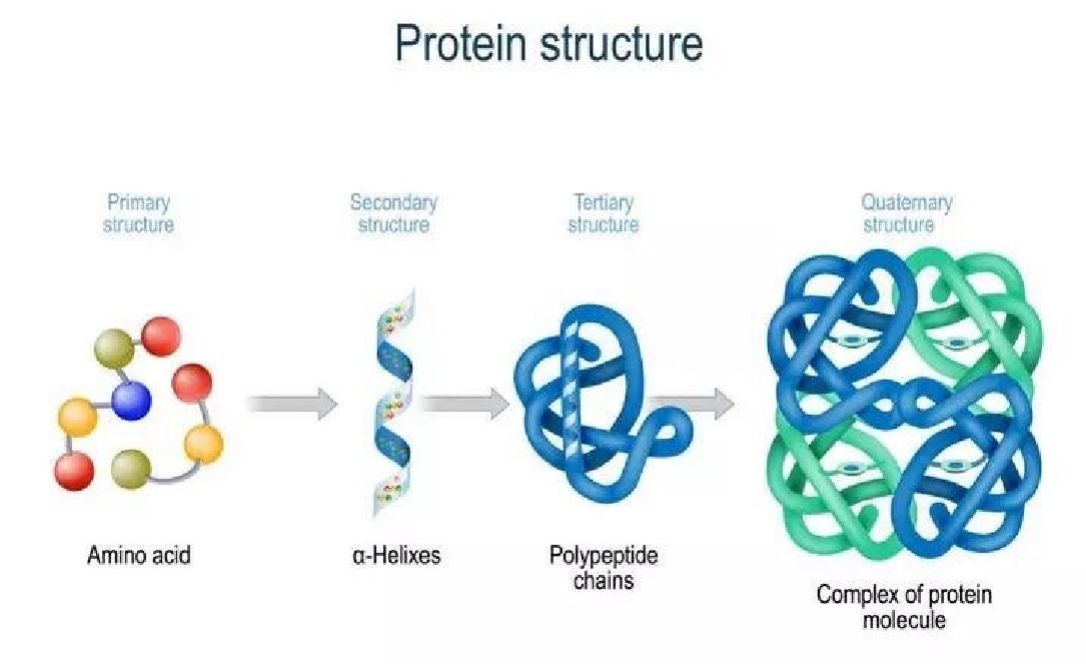
Types of bonds

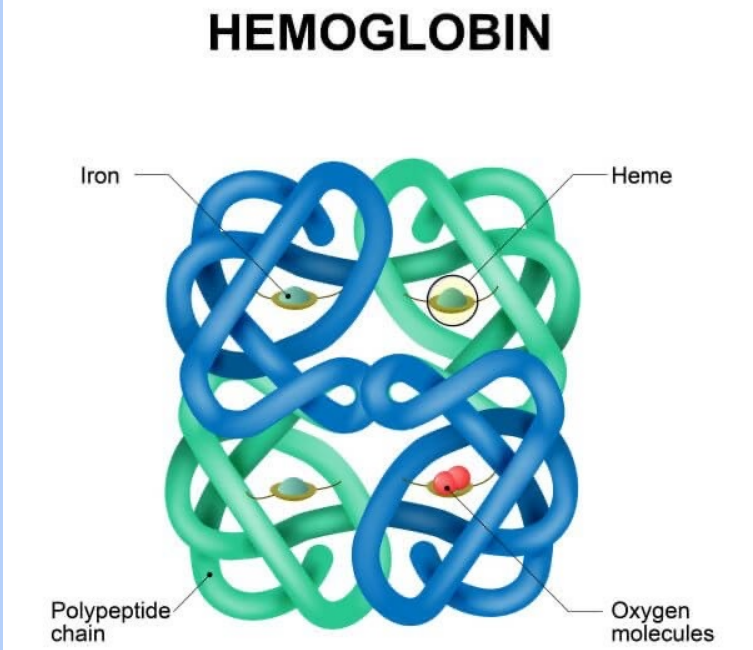
1. Hydrophobic interactions
2. Ionic bonds
3. Van der Waals interactions
4. Hydrogen bonds
5. Disulfide bridges

(Remember HIV in HD)

- The folding by the non-specific hydrophobic interactions, the burial of hydrophobic residues from water, the structure is stable only when the parts of a protein domain are locked into place by specific tertiary interactions

- The disulfide bonds are extremely rare in cytosolic proteins





Quaternary structure

- the three-dimensional structure consisting of the aggregation of two or more individual polypeptide chains (subunits) that operate as a single functional unit (multimer).
- The resulting multimer is stabilized by the same non-covalent interactions and disulfide bonds as in tertiary structure. There are many possible quaternary structure organizations.
- Ex. Hemoglobin

Summary of bonds/interactions

	PRIMARY STRUCTURE	SECONDARY STRUCTURE	TERTIARY STRUCTURE	QUATERNARY STRUCTURE
TYPES OF BONDS	Peptide bonds	Hydrogen bonds	**H**ydrophobic interactions **I**onic bonds **V**an der Waals interactions **H**ydrogen bonds **D**isulfide bridges (Remember HIV in HD)	Non-covalent bonds (hydrogen bonds and van der Waals forces between nonpolar side chains) Disulfide bridges