Protein Structure

Ola Amland

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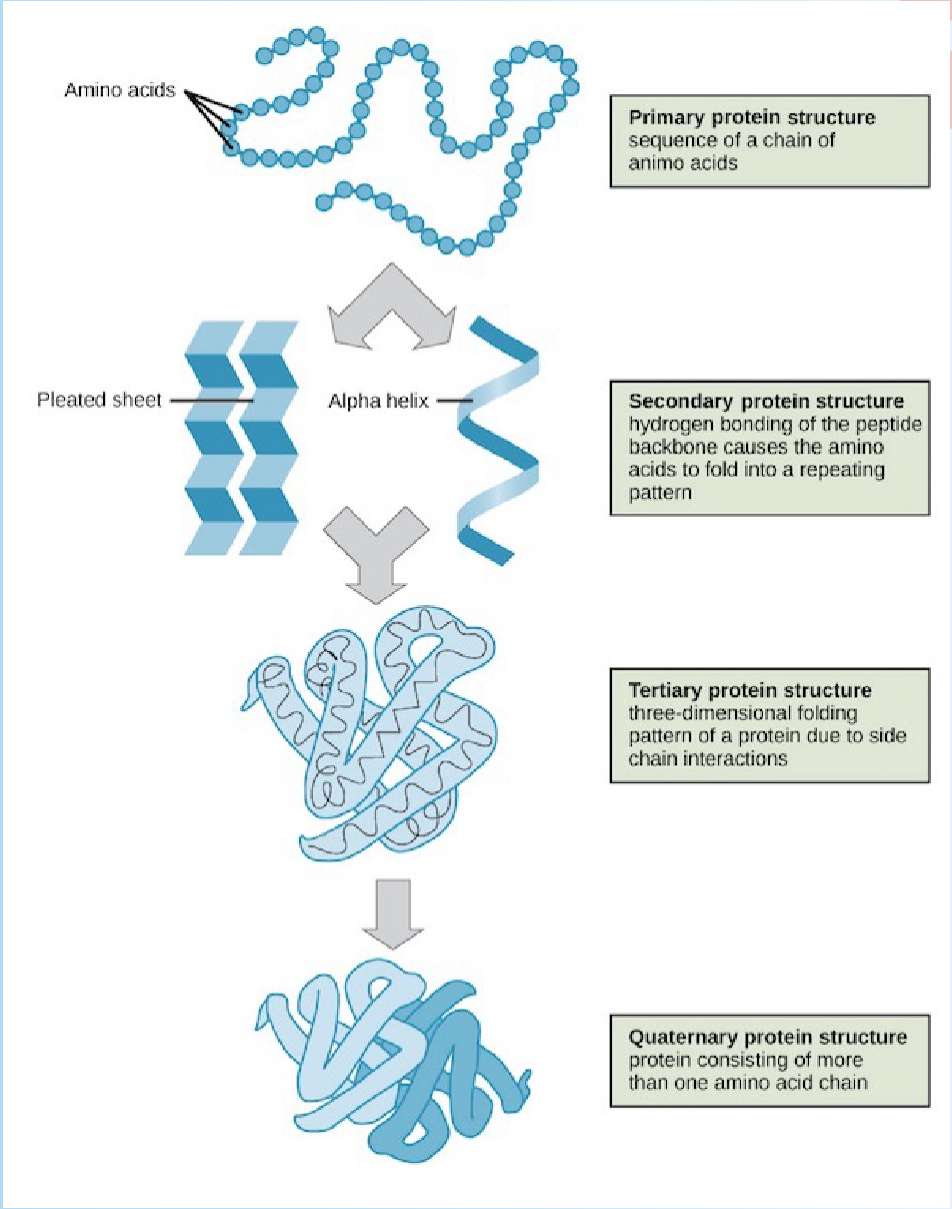
Protein structure

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



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Primary Structure

The primary structure = sequence of amino acids in the polypeptide chain.

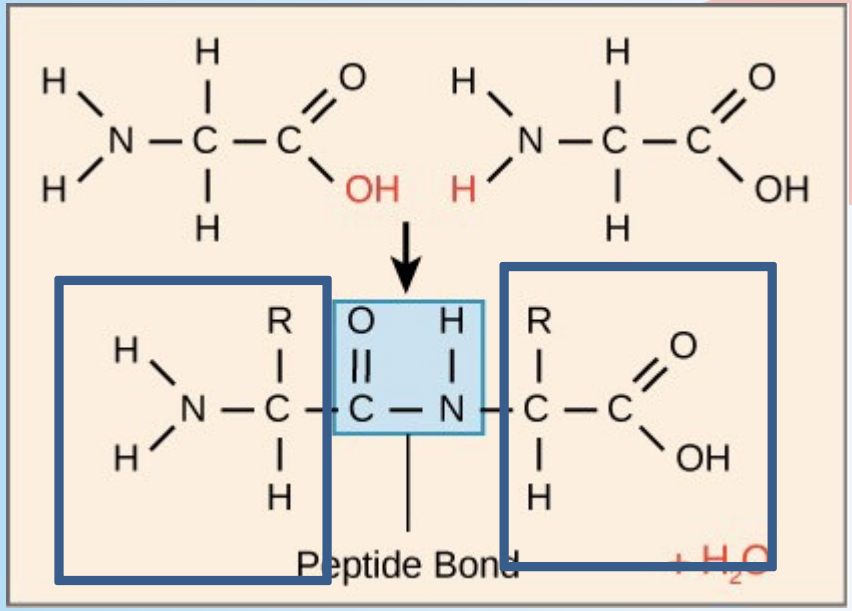
The two ends

- Amino terminus (N-terminus)
- Carboxyl terminus (C-terminus)
- The sequence is read from N→C

Bonds

Peptide bonds – between C and N terminus of sequential AA

Condensation Reaction



Determined by the gene corresponding to the protein

All of the info about folding is in the primary sequence

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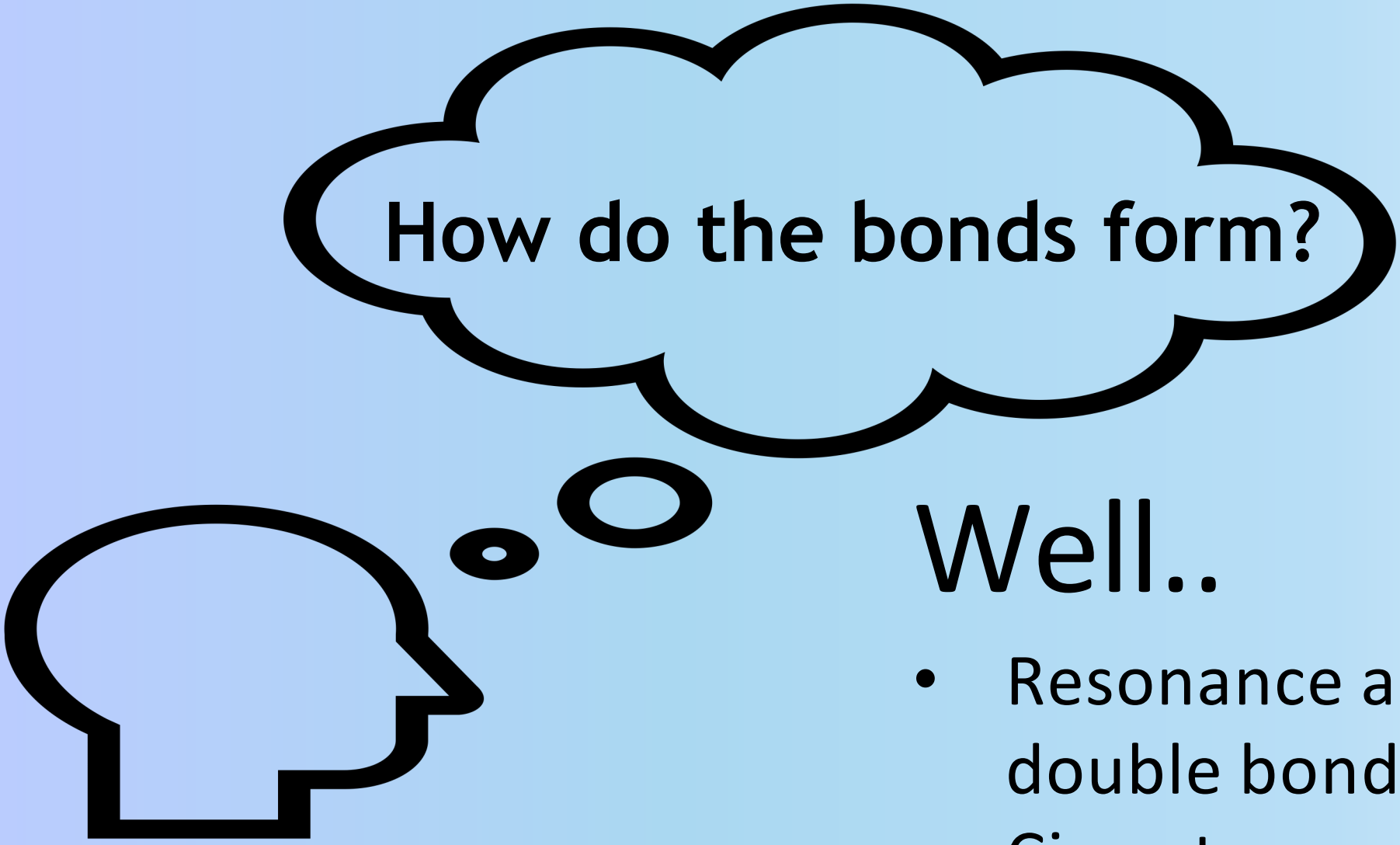

Well..

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

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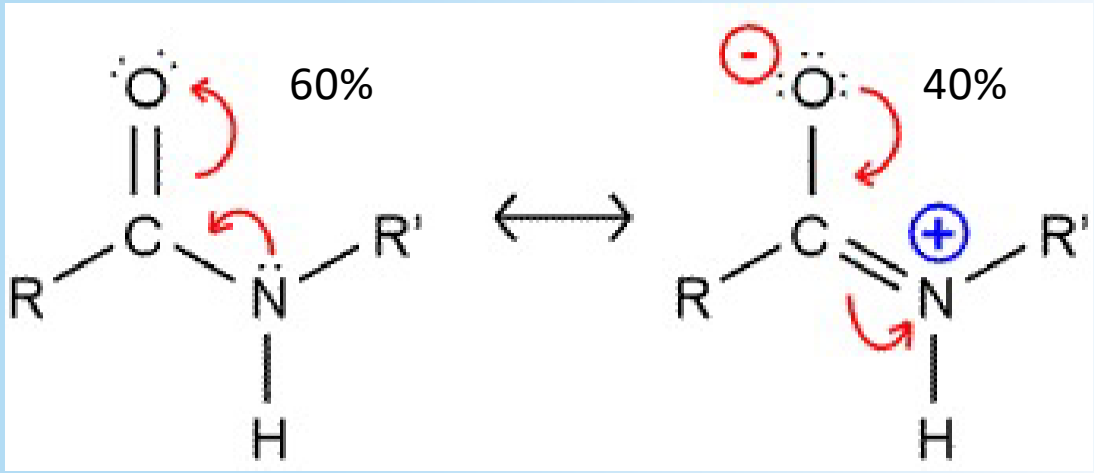
Partial Double Bonds

- 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.

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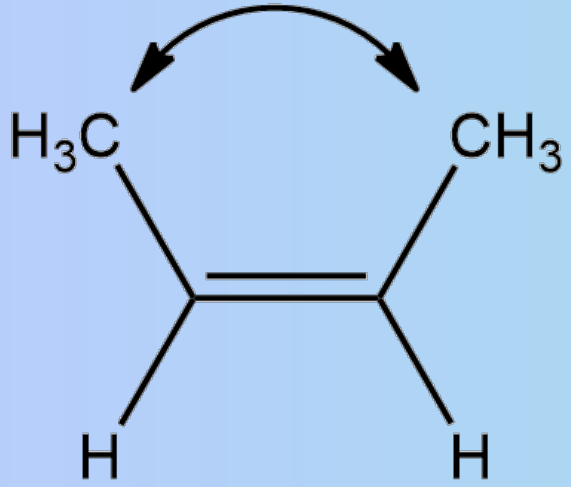
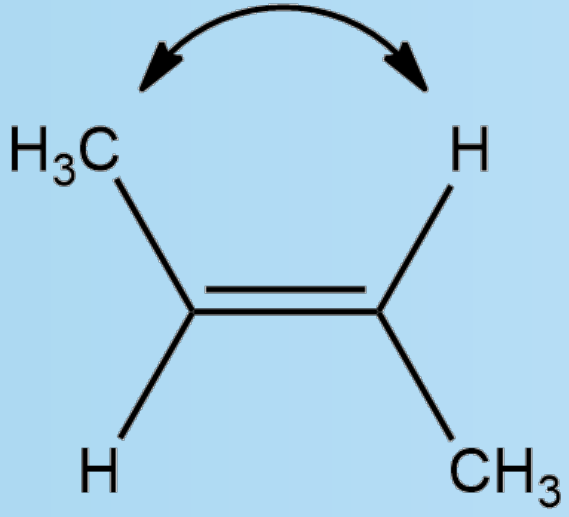
Cis and trans configuration

greater steric repulsion

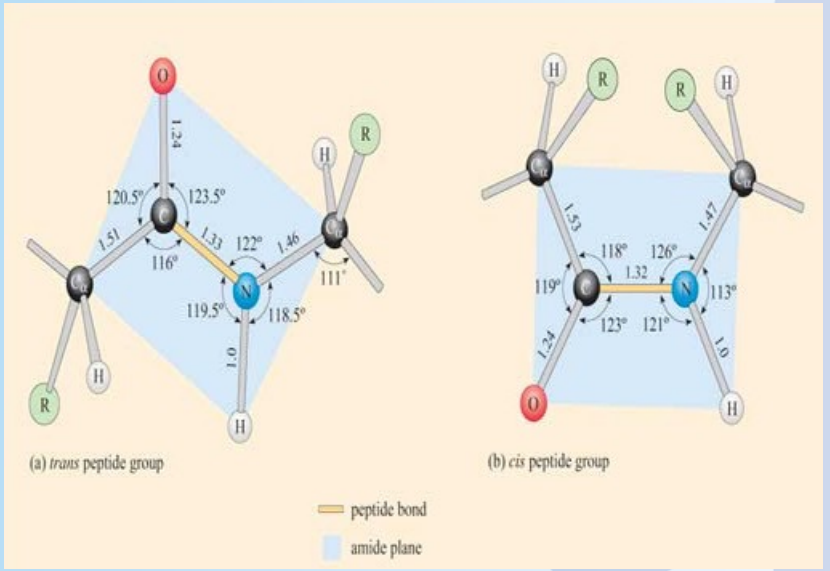


***cis* isomer**

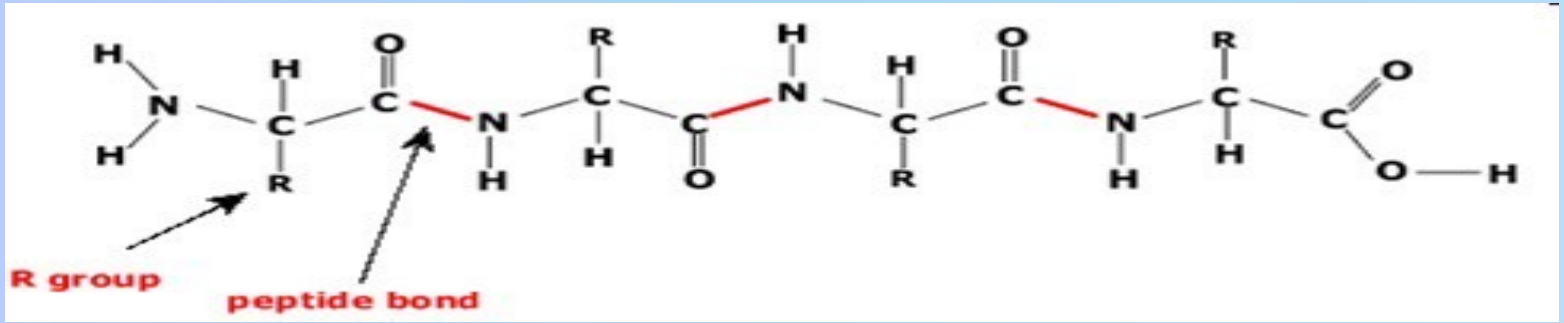
less steric repulsion

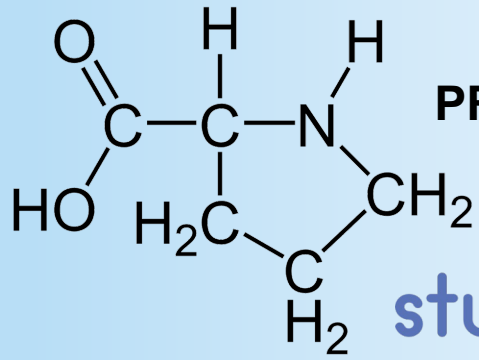


***trans* isomer**



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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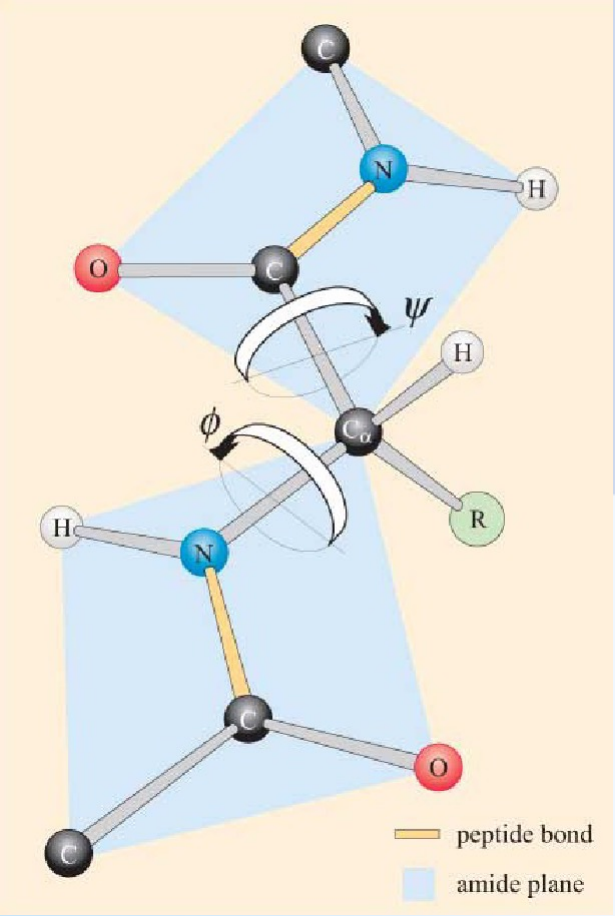
Steric Hinderance and Rotation

- **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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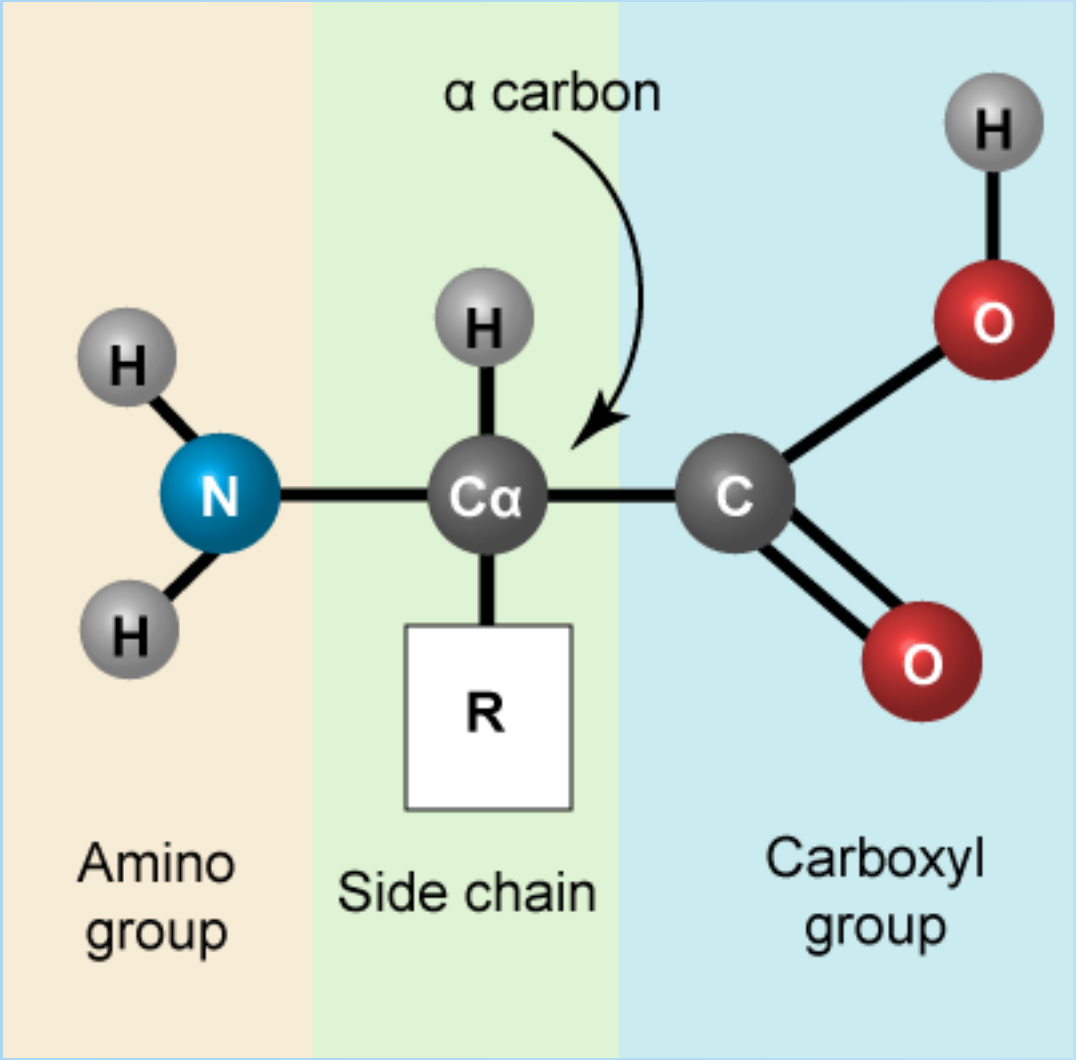
α carbon
H
O
H
H
N
Cα
C
O
H
R
Amino group
Side chain
Carboxyl group

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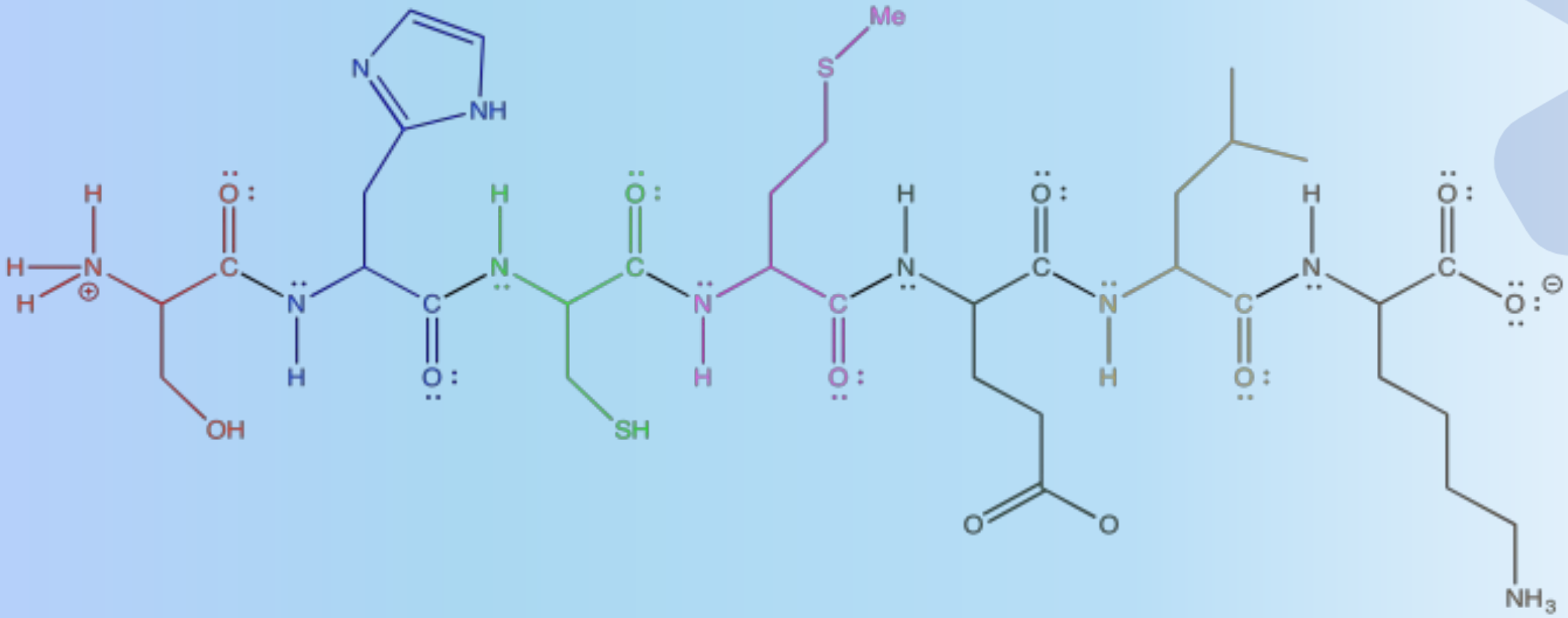
Rigid planar structure!



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

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Secondary structure

HYDROGEN BONDS
- H----F
- H----O
- H----N

- The main regular types of secondary structure:
  - the *α-helix*
  - *β-strand or β-sheets*

- 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.

Irregular types of secondary structure:
- Bends
- Loops
- Turns
- Motifs
- Coils

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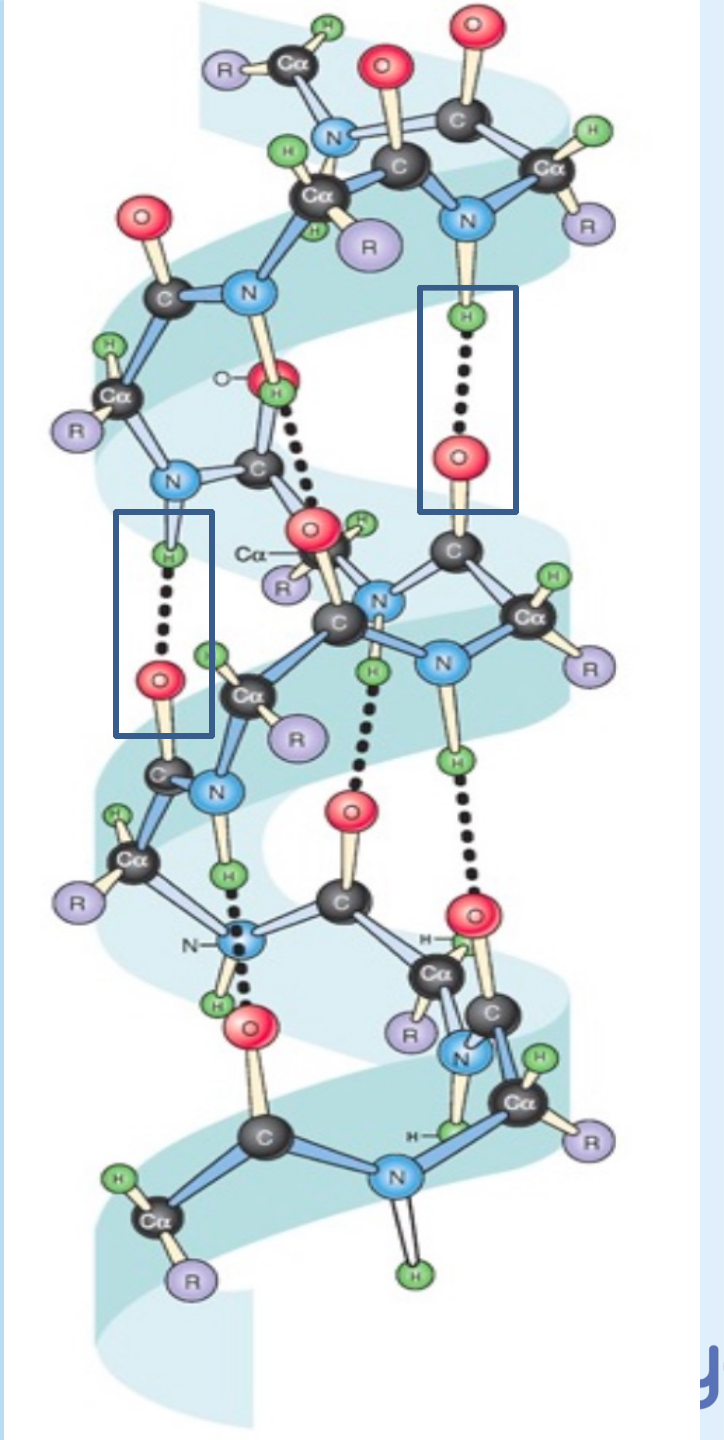
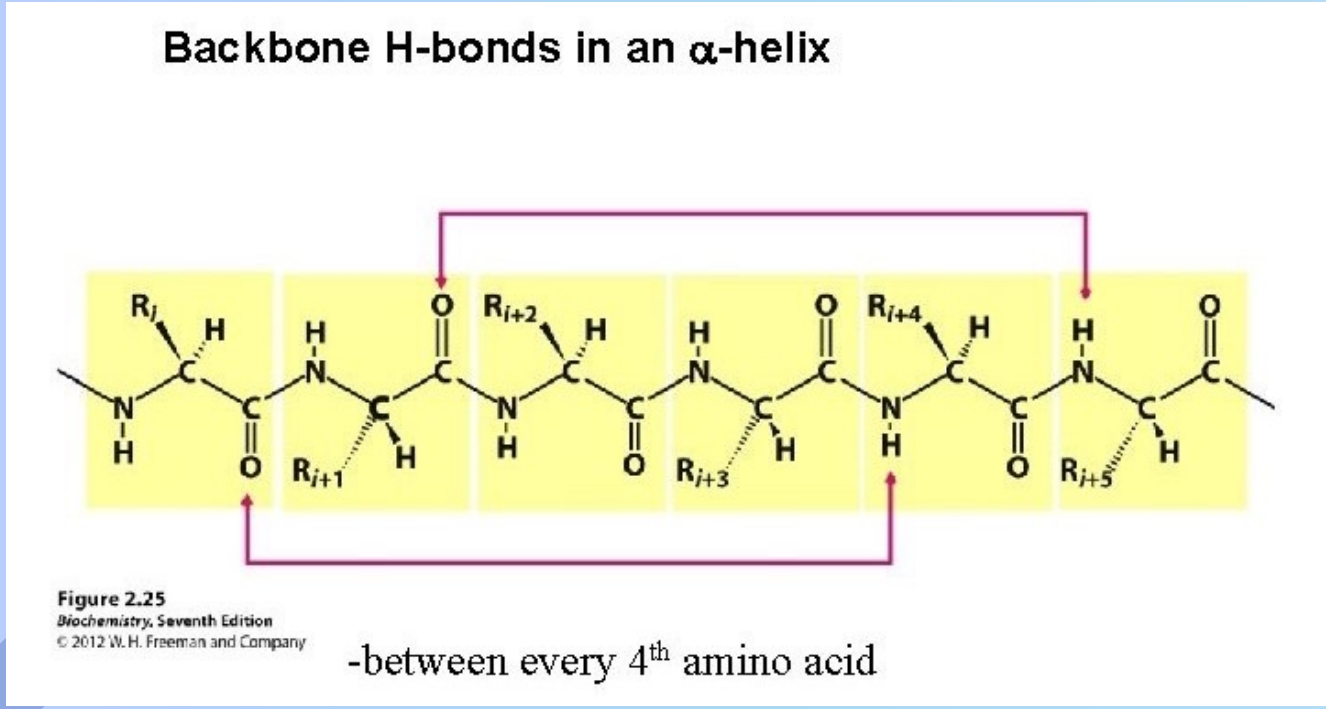
Alpha Helix

- 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

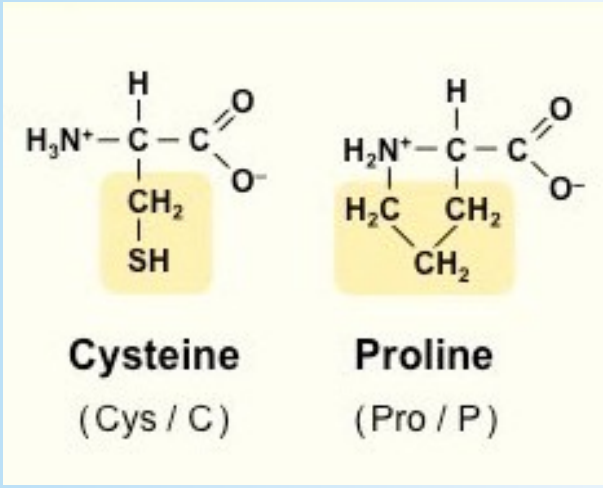


Alpha helix

High yield: Proline is a “helix-breaker” and is generally not found in a-helical regions of proteins



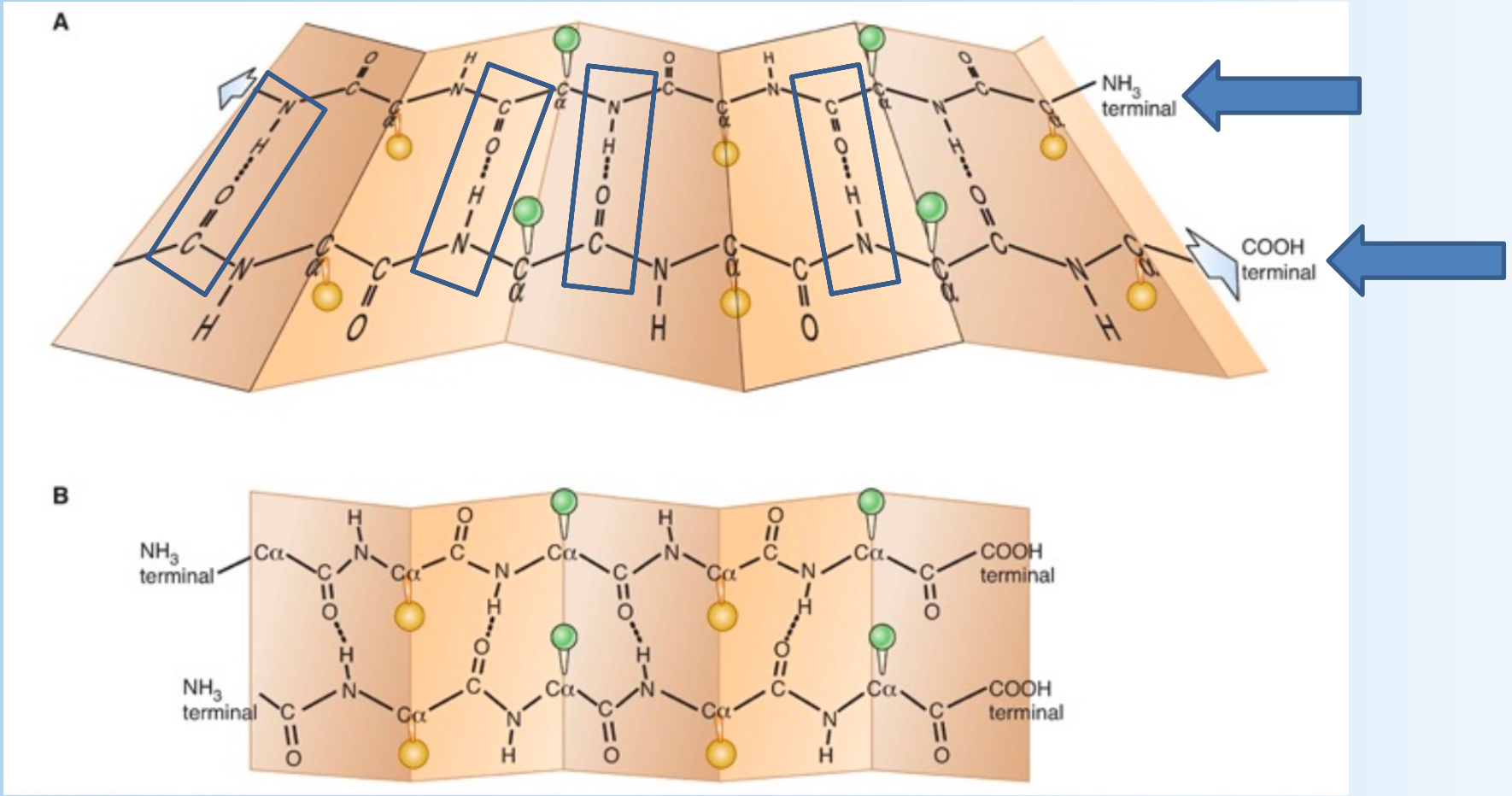
Proline cannot form the necessary bond angles to fit within an alpha helix



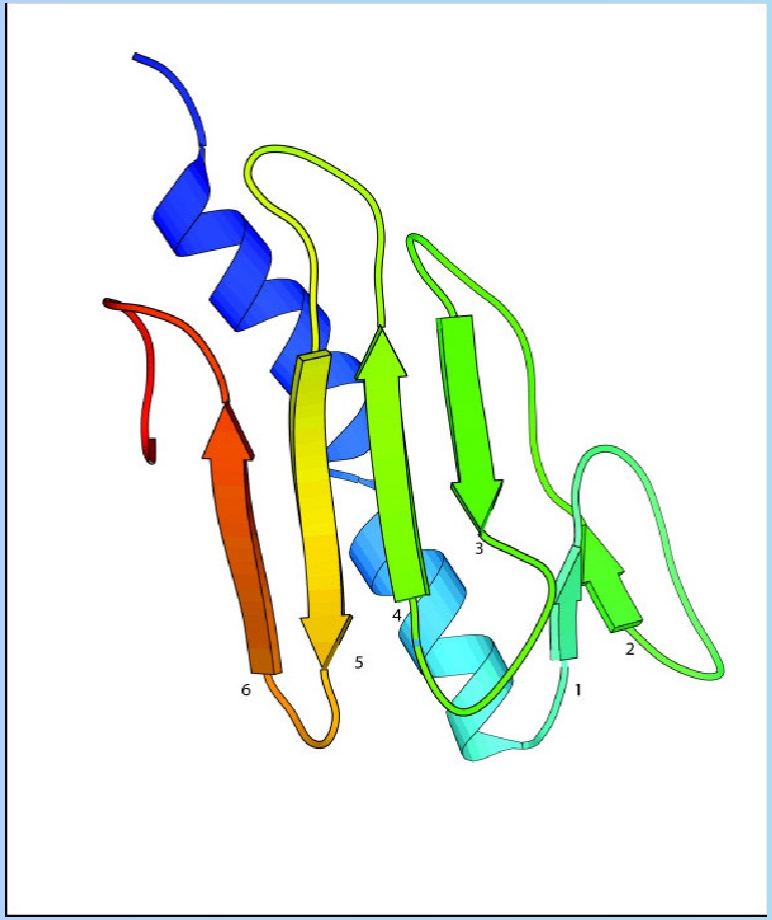
Beta-pleated sheets

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

- Parallel vs antiparallel



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.

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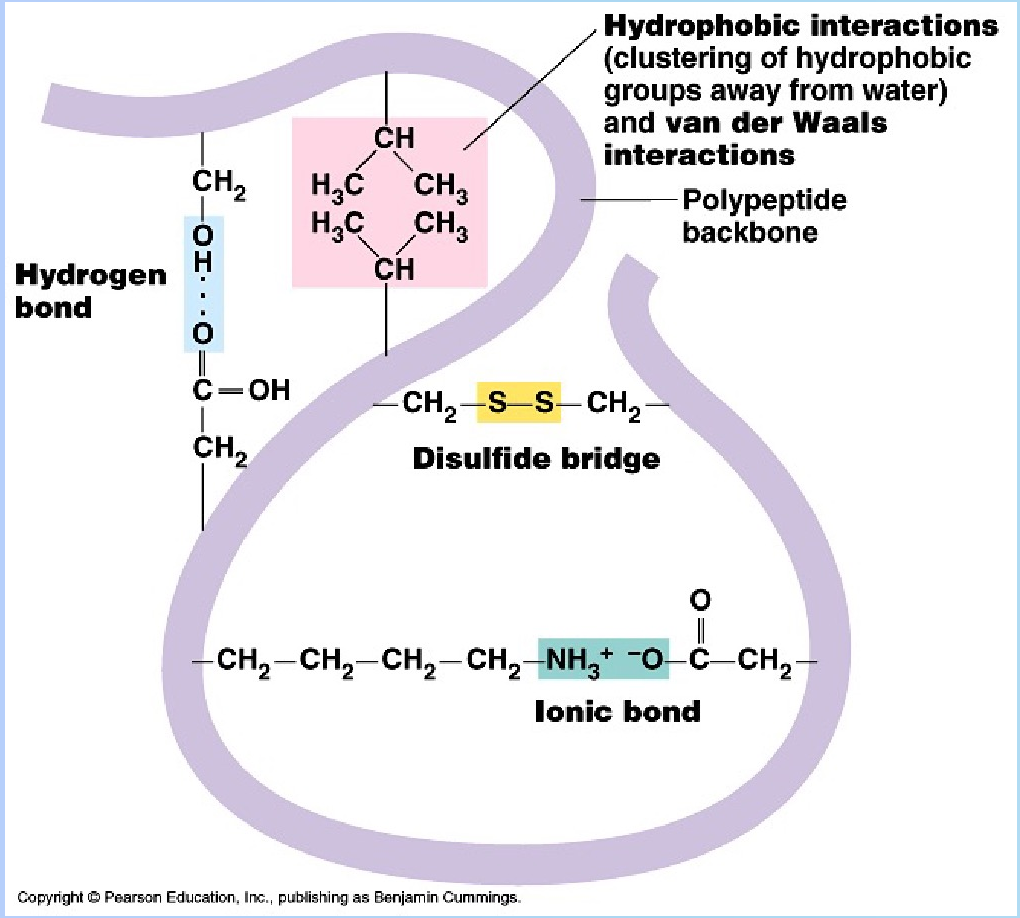
Bonds



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

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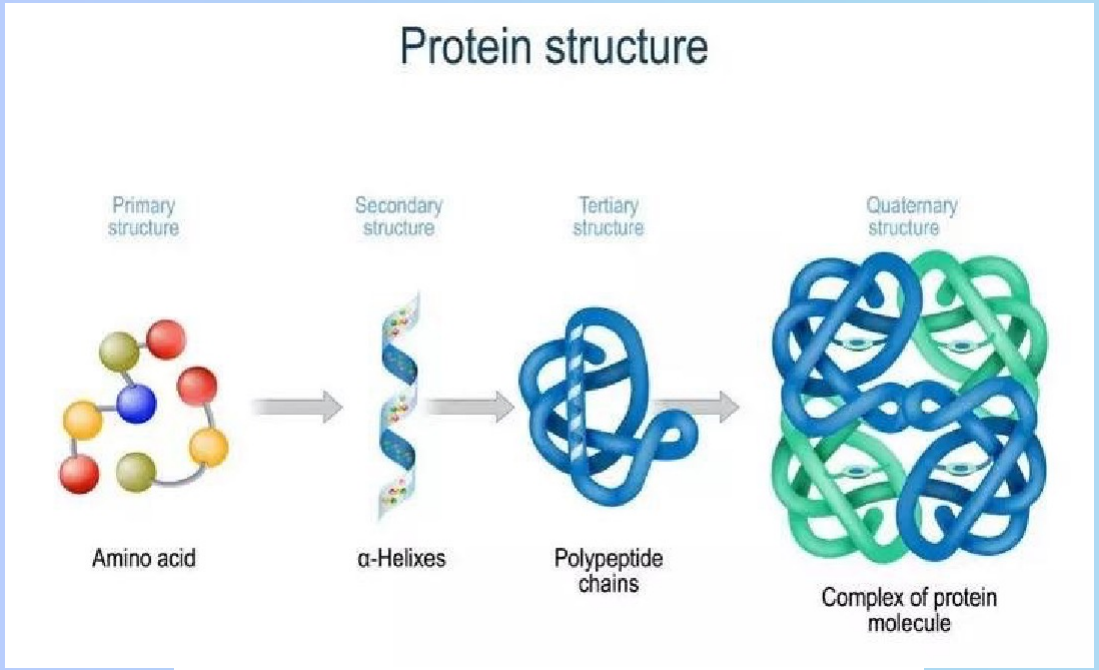

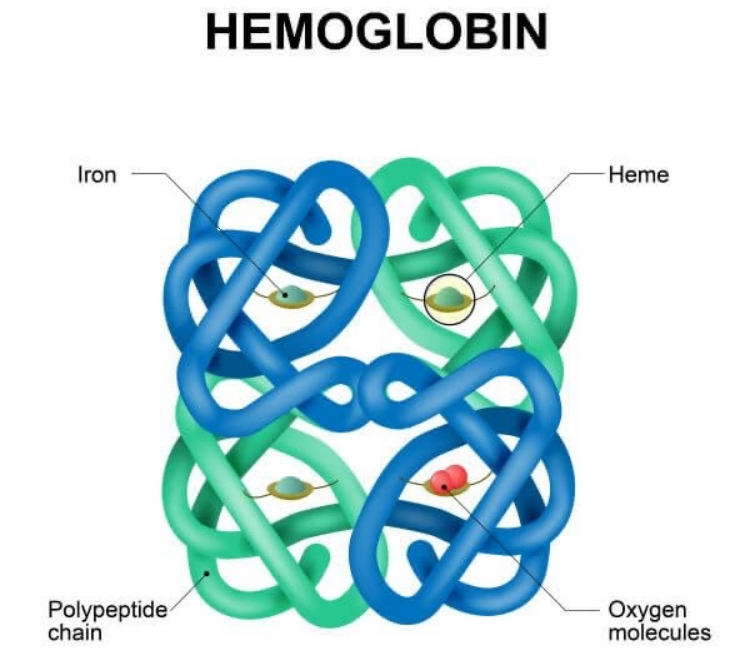

Quaternary structure

- 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

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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 • Occasional ionic bonds or salt bridges Disulfide bridges (rare)

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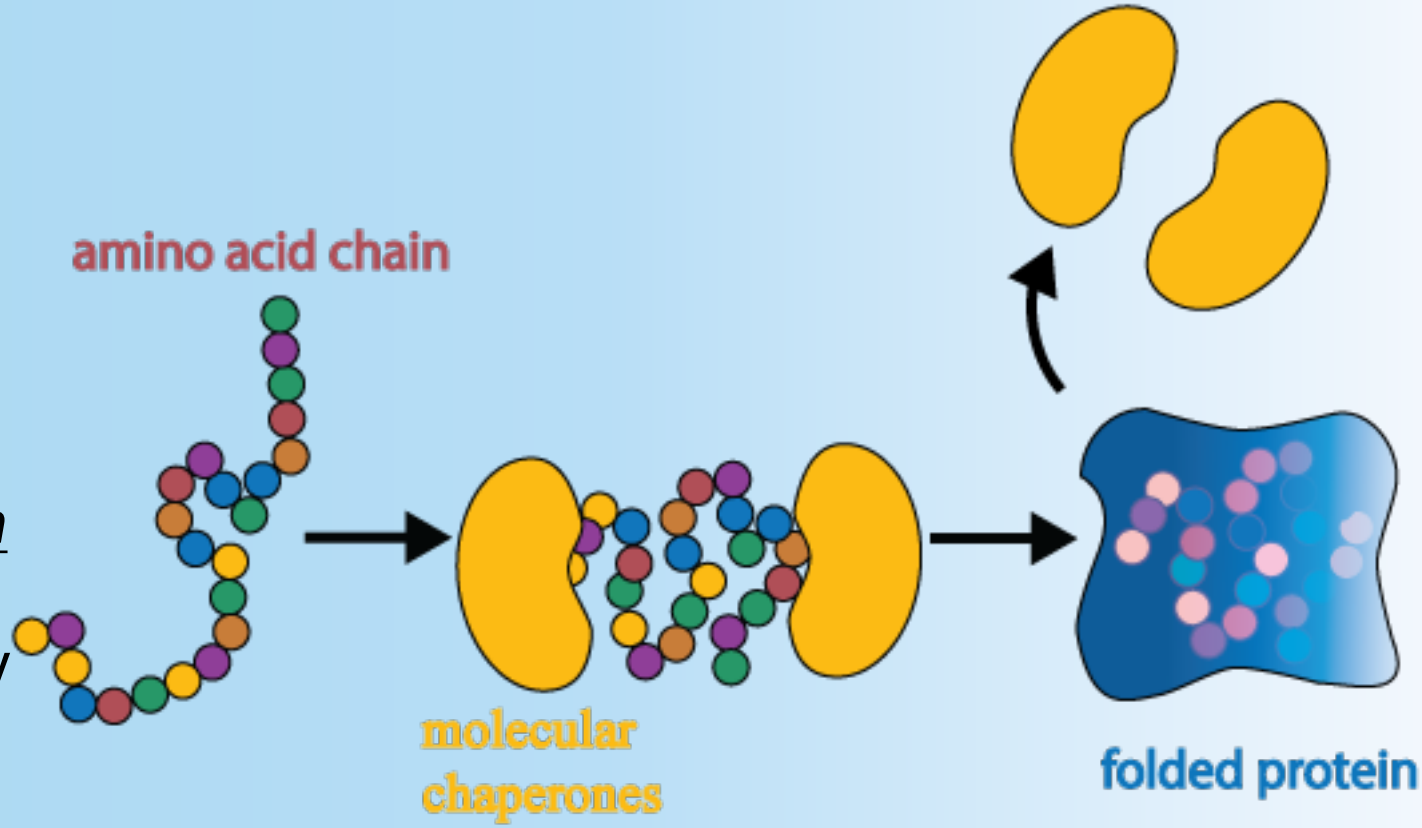
Protein folding

- Every molecule of the same protein folds into the same stable three-dimensional structure, this shape is known as *native conformation*
- Heat shock proteins – use energy (ATP) to assist in the folding process
  - HSP60 - *Chaperons*



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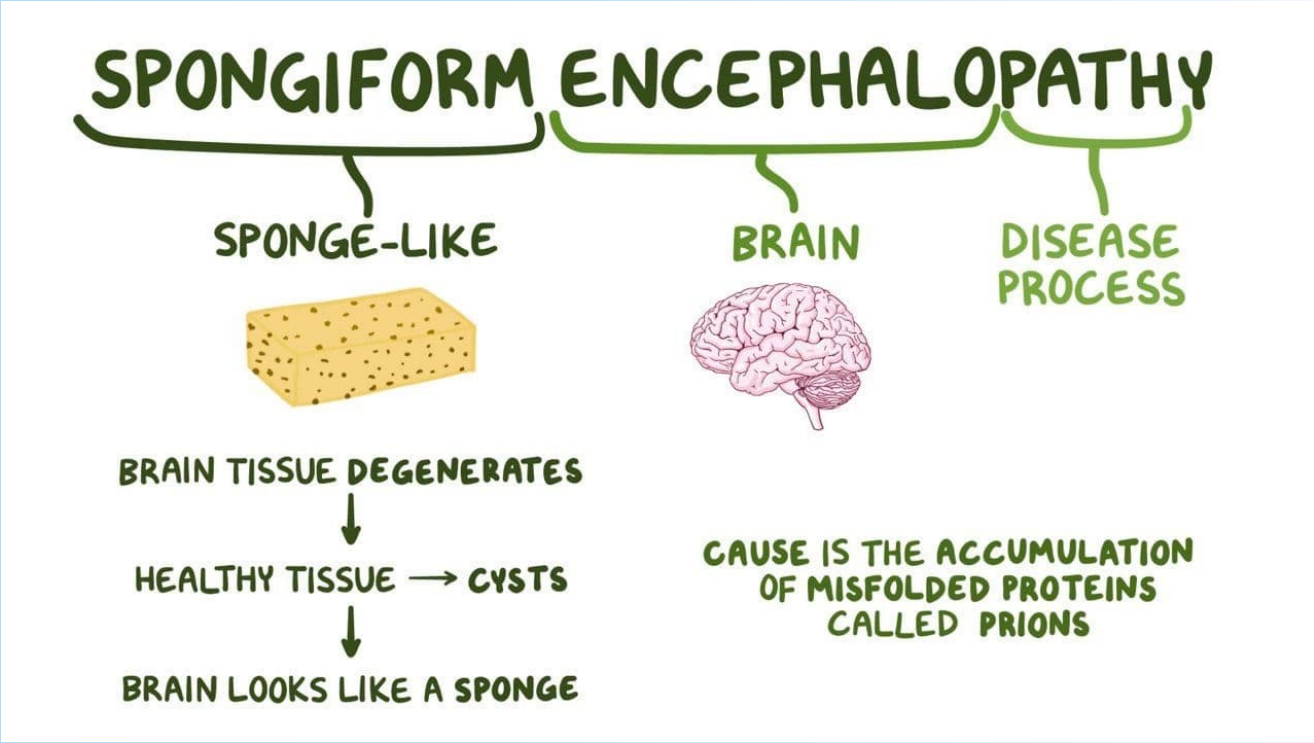
Prions

Prions: Causes misfolding of proteins

“Proteinaceous infectious agent”

Causes Creutzfeld-Jakob disease (CJD) “Mad cow” disease

Protein aggregates and amyloid plaques are formed



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