جامعة المستقبل
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كلية العلـــوم
قـسـم الادلة الجنائية

المحاضرة الثانية

The Structure and Functions of Proteins

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The Structure and Functions of Proteins

The many functions of proteins

- Mechanoenzymes: myosin, actin
- Rhodopsin: allows vision
- Globins: transport oxygen
- Antibodies: immune system
- Enzymes: pepsin, renin, carboxypeptidase A
- Receptors: transmit messages through membranes
- Vitelogenin: molecular velcro
  - And hundreds of thousands more…

Complex Chemistry Tutorial

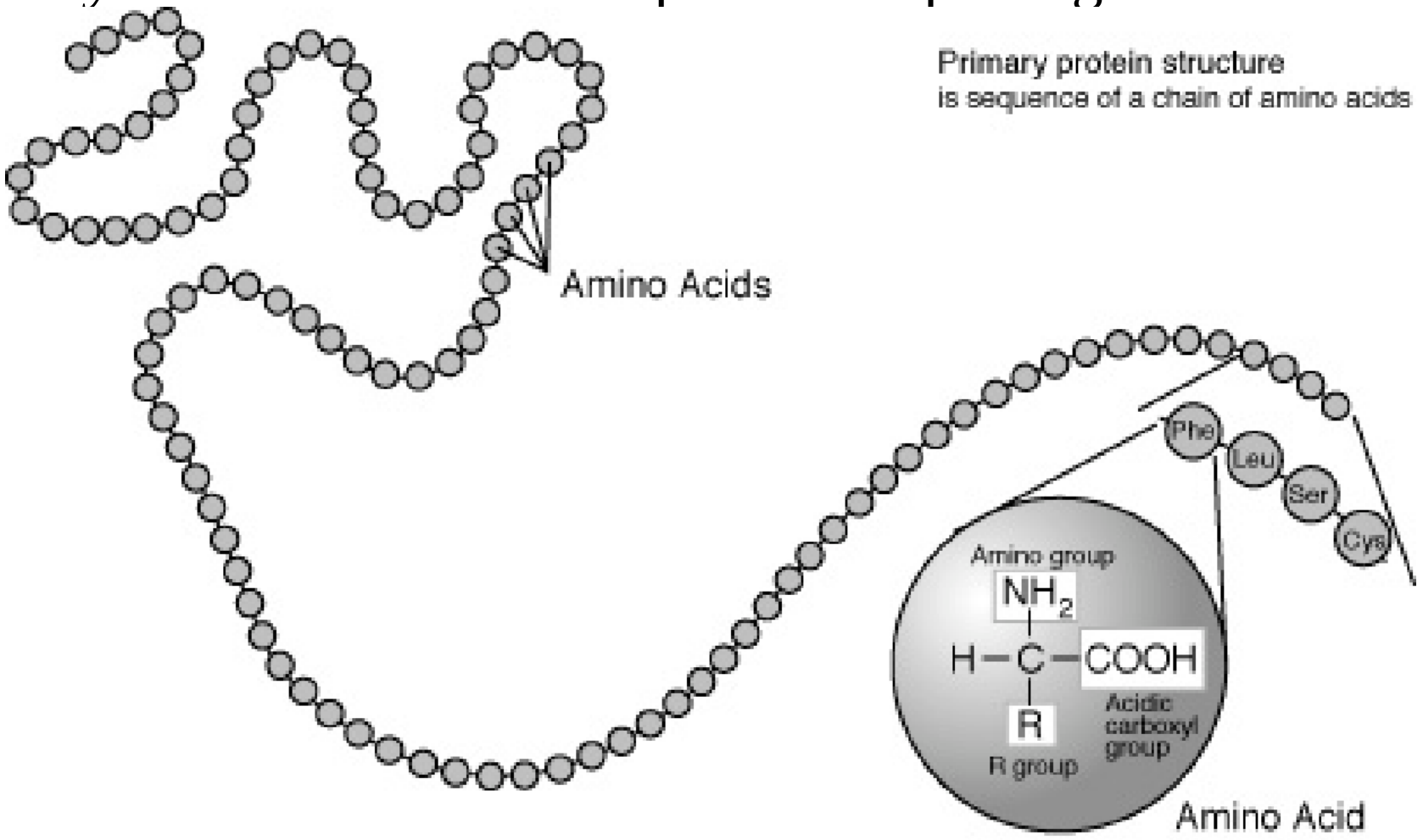
- Molecules are made of atoms!
- There is a lot of hydrogen out there!
  - Atoms make a "preferred" number of *covalent* (strong) bonds
    - C – 4
    - N – 3
    - O, S – 2
- Atoms will generally "pick up" enough hydrogens to "*fill their valence capacity" in vivo.*
- Molecules also "prefer" to have a neutral charge

Biochemistry

- In the context of a protein…
  - Oxygen tends to exhibit a slight negative charge
  - Nitrogen tends to exhibit a slight positive charge
  - Carbon tends to remain neutral/uncharged
- Atoms can "share" a hydrogen atom, each making "part" of a covalent bond with the hydrogen
  - Oxygen: H-Bond donor or acceptor
  - Nitrogen: H-Bond donor
  - Carbon: Neither

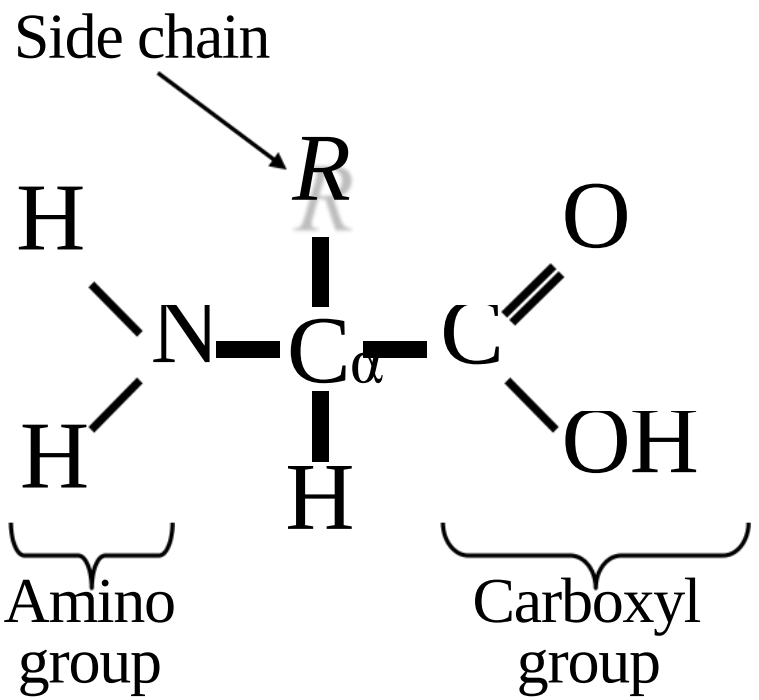
Proteins are chains of amino acids

- *Polymer* – a molecule composed of repeating units

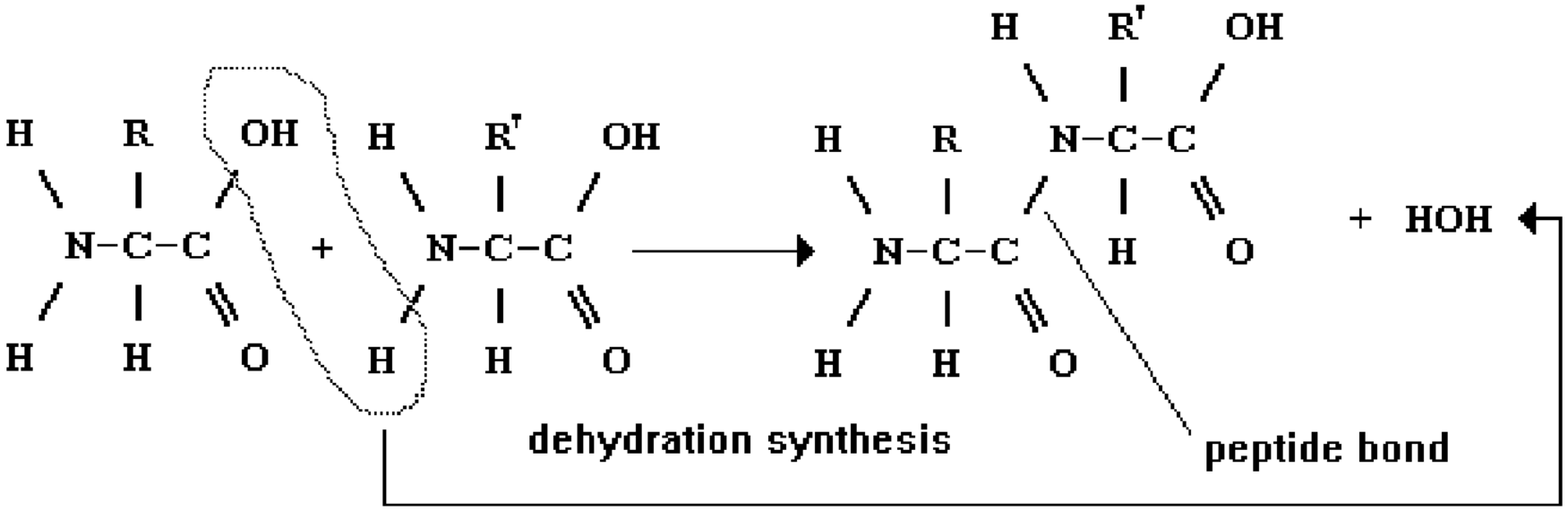


Amino acid composition

- Basic Amino Acid Structure:
  - The side chain, R, varies for each of the 20 amino acids



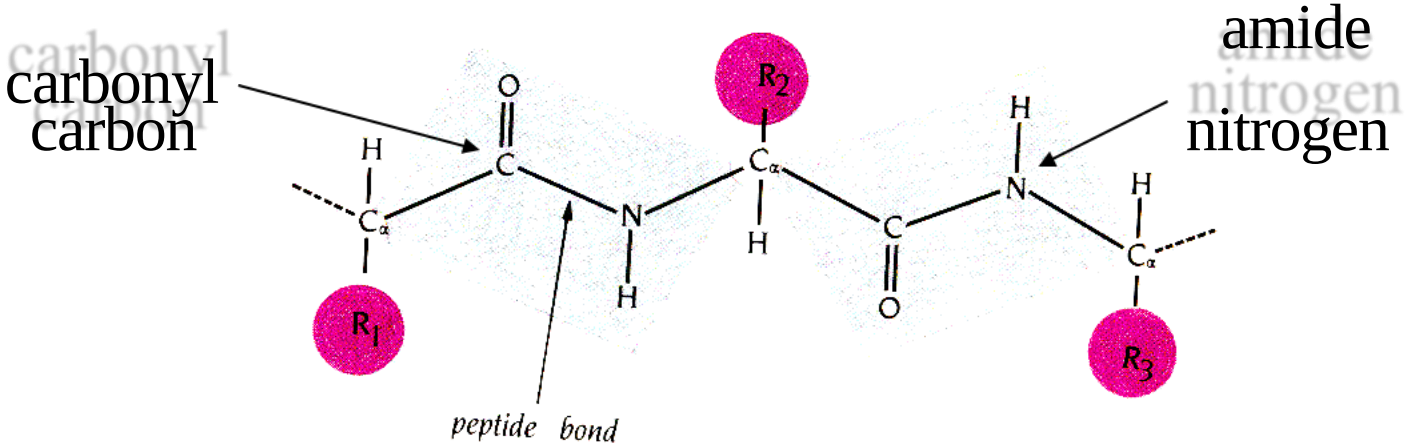
The Peptide Bond



- Dehydration synthesis
- Repeating backbone: N–Cα –C –N–Cα –C
  (C: O; C: O)
  - Convention – start at *amino terminus* and proceed to *carboxy terminus*

Peptidyl polymers

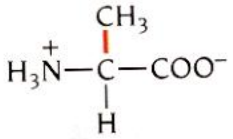
- A few amino acids in a chain are called a *polypeptide*. A *protein* is usually composed of 50 to 400+ amino acids.
- Since part of the amino acid is lost during dehydration synthesis, we call the units of a protein *amino acid* ***residues***.



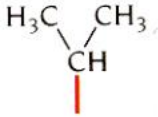
Side chain properties

- Recall that the electronegativity of carbon is at about the middle of the scale for light elements
  - Carbon does not make hydrogen bonds with water easily – *hydrophobic*
  - O and N are generally more likely than C to h-bond to water – *hydrophilic*
- We group the amino acids into three general groups:
  - Hydrophobic
  - Charged (positive/basic & negative/acidic)
  - Polar

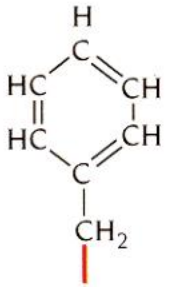
The Hydrophobic Amino Acids



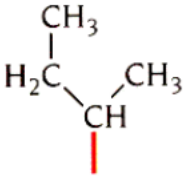
A Ala, Alanine



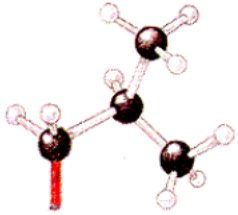
V Val, Valine

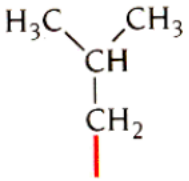


F Phe, Phenylalanine

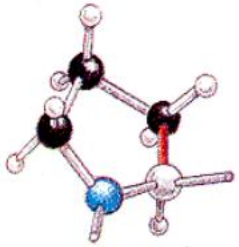


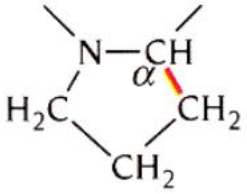
I Ile. Isoleucine





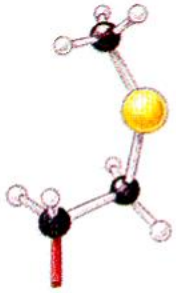
L Leu, Leucine

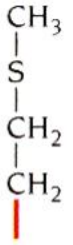




P Pro, Proline

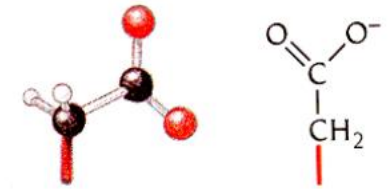
Proline severely limits allowable conformations!



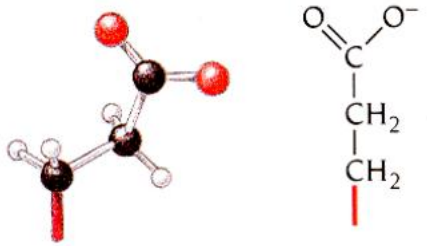


M Met, Methionine

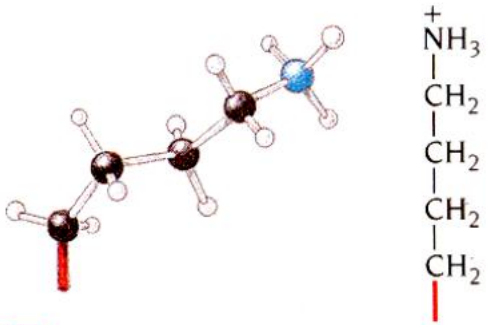
The Charged Amino Acids



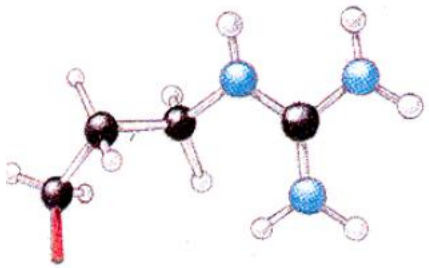
D Asp, Aspartic acid

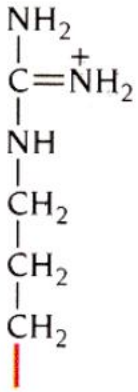


E Glu, Glutamic acid



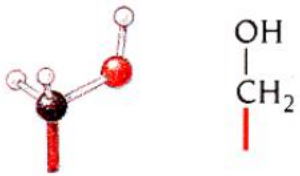
K Lys, Lysine



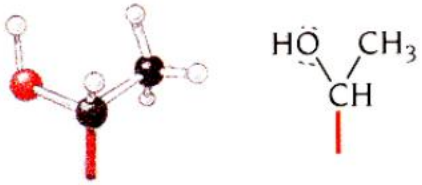


R Arg, Arginine

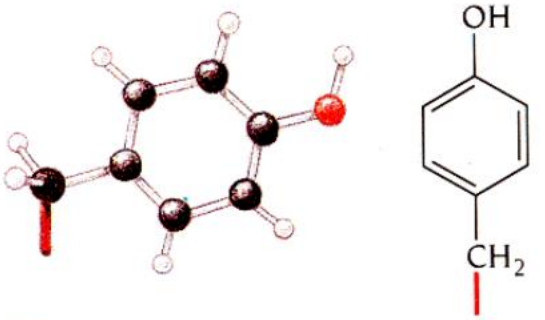
The Polar Amino Acids



S Ser, Serine

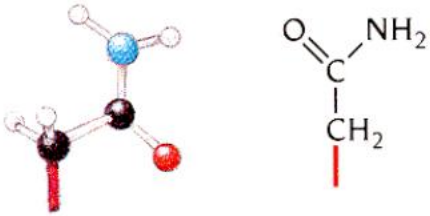


T Thr, Threonine

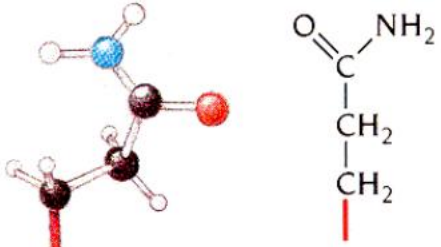


Y Tyr, Tyrosine

C Cys, Cysteine

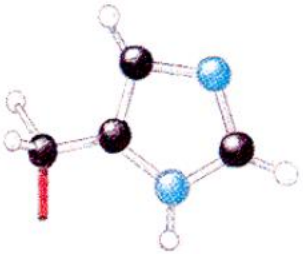


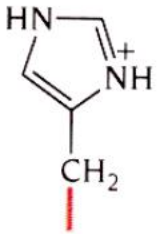
N Asn, Asparagine



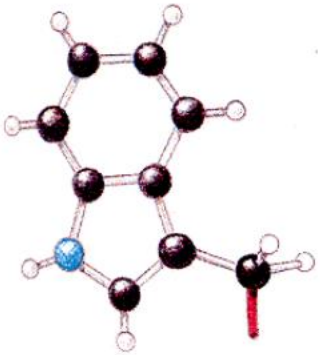
Q Gln, Glutamine

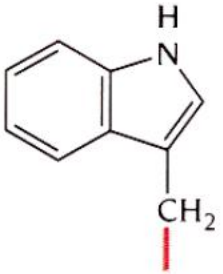
More Polar Amino Acids





H His, Histidine



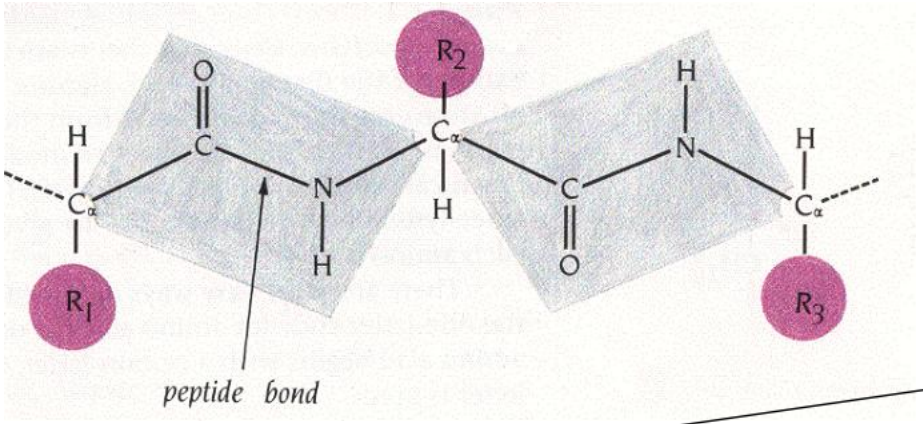


W Trp, Tryptophan

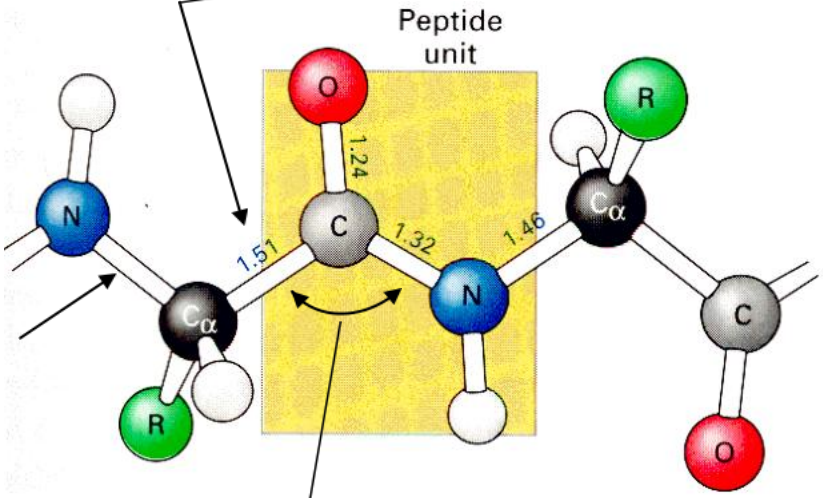
And then there's…

G Gly, Glycine

Planarity of the peptide bond

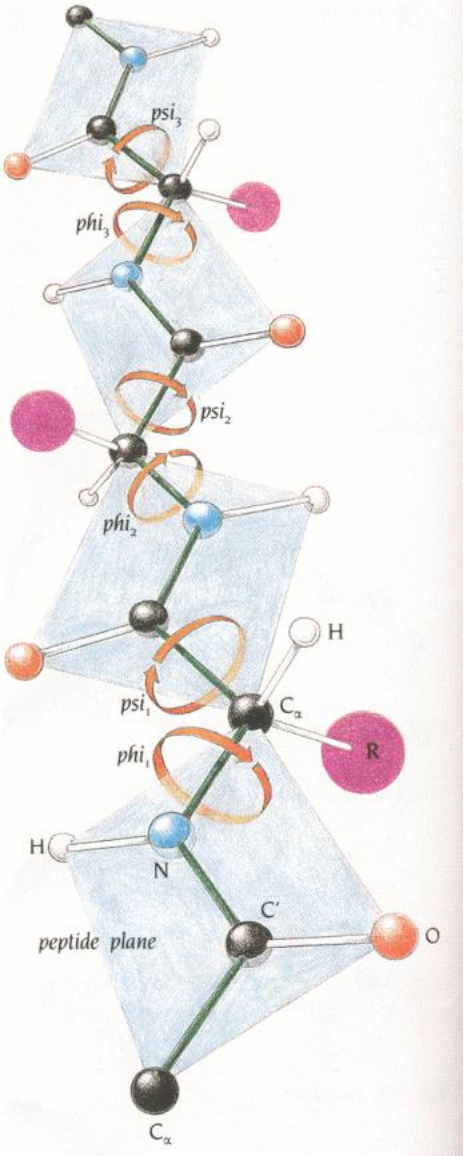


Psi (ψ) – the angle of rotation about the Cα-C bond.



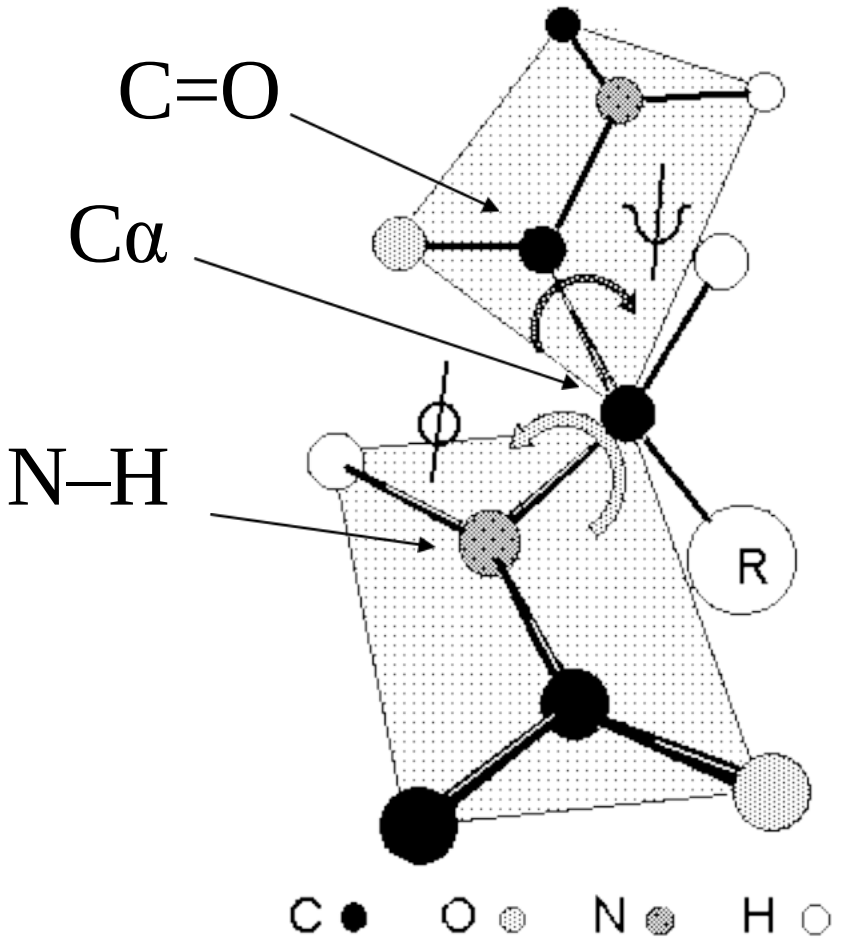
Phi (φ) – the angle of rotation about the N-Cα bond.

The planar bond angles and bond lengths are fixed.

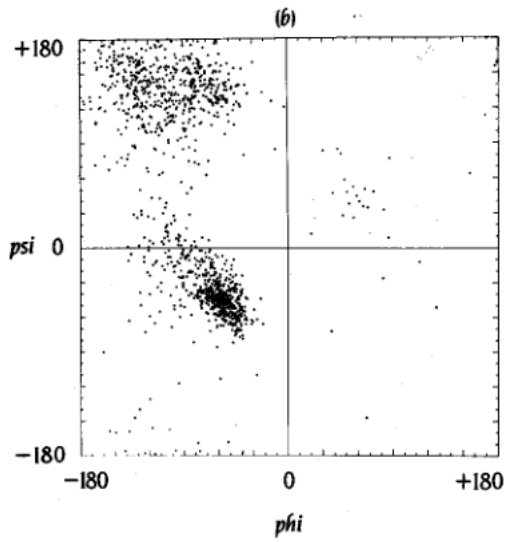


Phi and psi

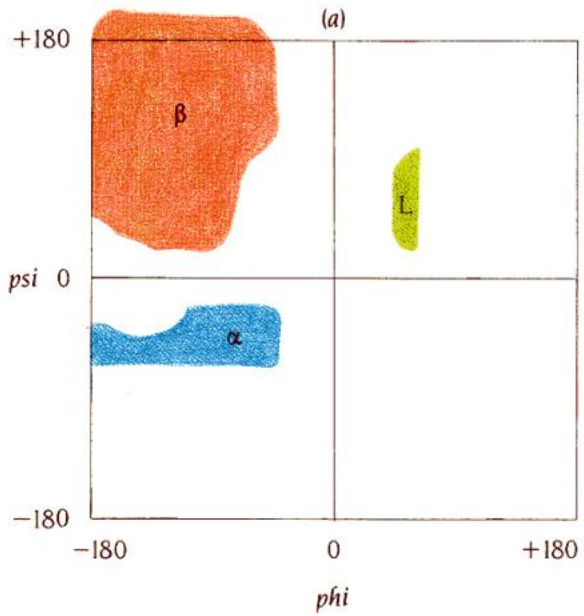
- φ = ψ = 180° is extended conformation
- φ : Cα to N–H
- ψ : C=O to Cα



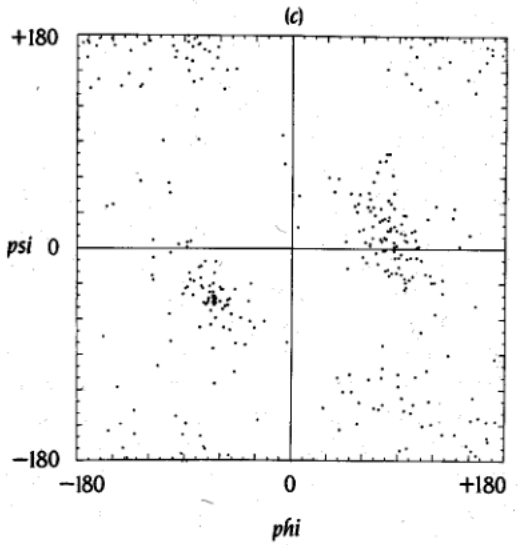
The Ramachandran Plot



Observed (non-glycine)



Calculated



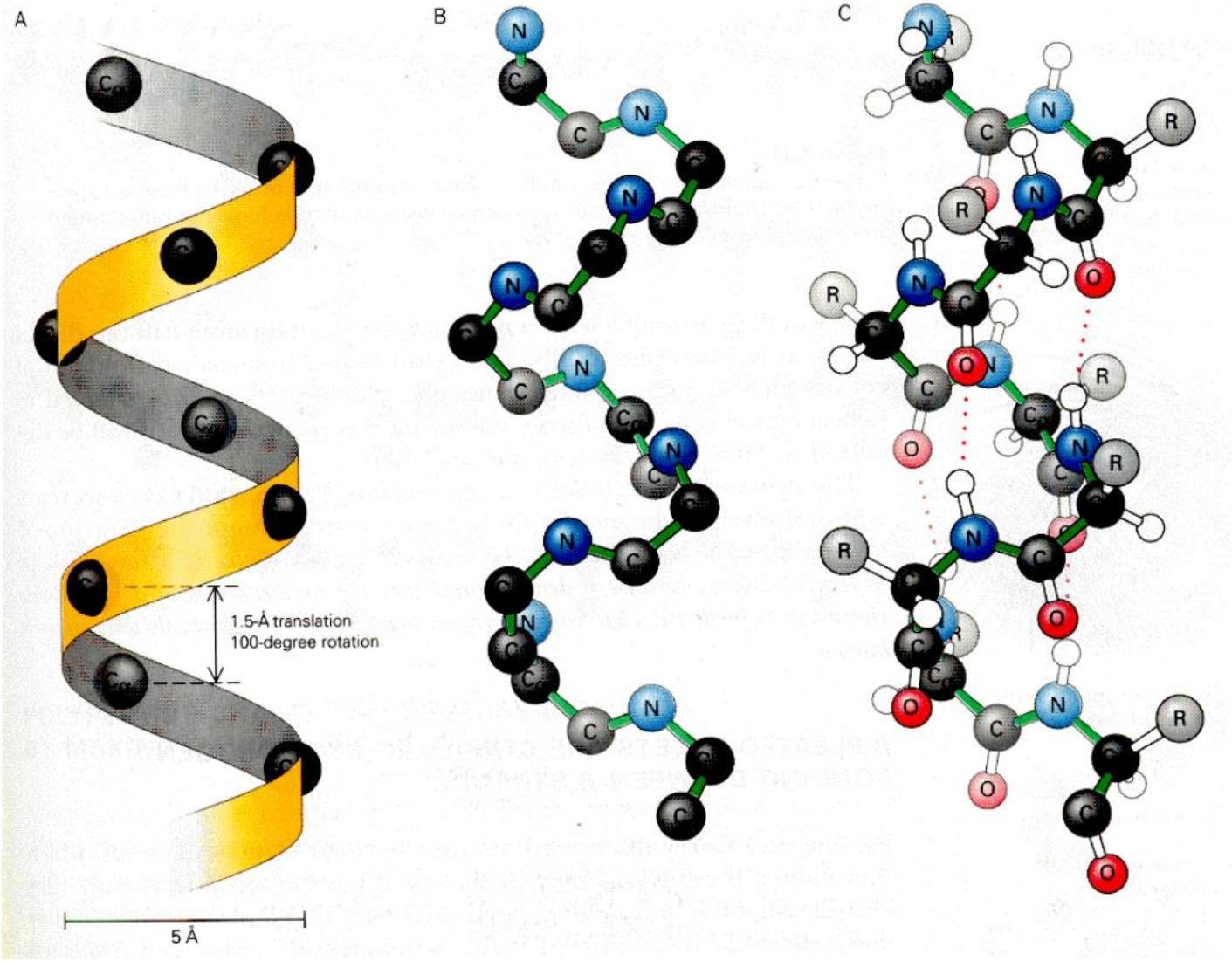
Observed (glycine)

- G. N. Ramachandran – first calculations of *sterically* allowed regions of phi and psi
- Note the structural importance of glycine

Primary & Secondary Structure

- Primary structure = the linear *sequence* of amino acids comprising a protein:
  AGVGTVPMTAYGNDIQYYGQVT…
- Secondary structure
  - Regular patterns of hydrogen bonding in proteins result in two patterns that emerge in nearly every protein structure known: the α-*helix* and the β-*sheet*
  - The location of direction of these periodic, repeating structures is known as the *secondary structure* of the protein

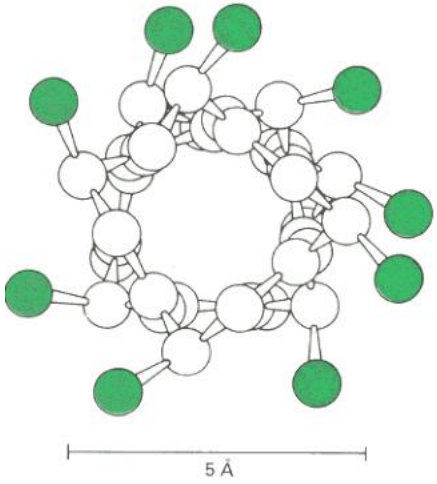
The alpha helix

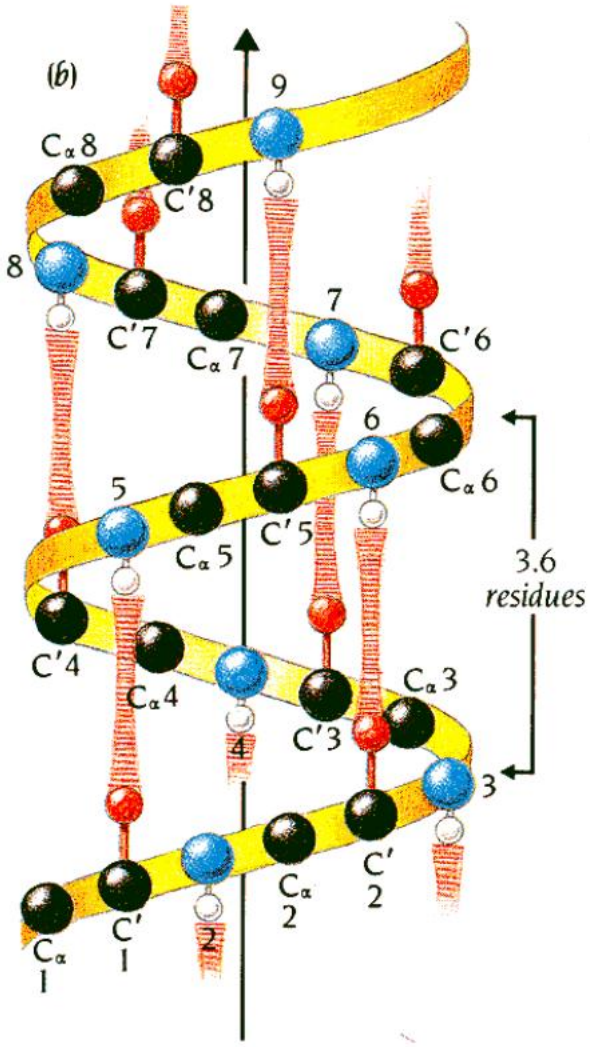


$\varphi \approx \psi \approx -60°$

Properties of the alpha helix

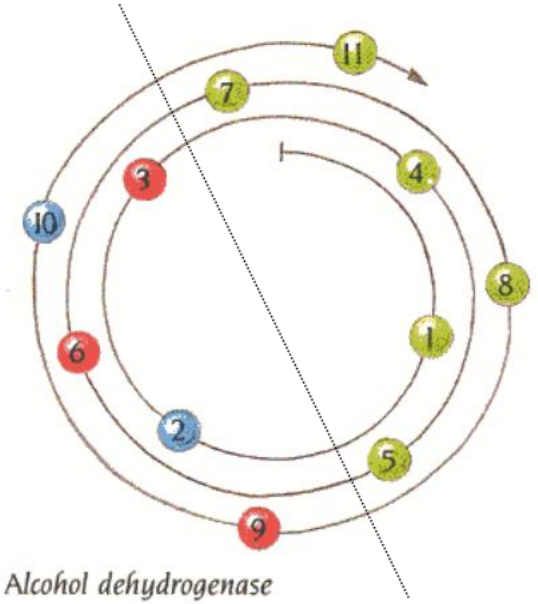
- $\varphi \approx \psi \approx -60°$
- Hydrogen bonds between C=O of residue *n*, and NH of residue *n*+4
- 3.6 residues/turn
- 1.5 Å/residue rise
- 100°/residue turn





Properties of α-helices

- 4 – 40+ residues in length
- Often *amphipathic* or "dual-natured"
  - Half hydrophobic and half hydrophilic
  - Mostly when surface-exposed
- If we examine many α-helices, we find trends…
  - Helix formers: Ala, Glu, Leu, Met
  - Helix breakers: Pro, Gly, Tyr, Ser

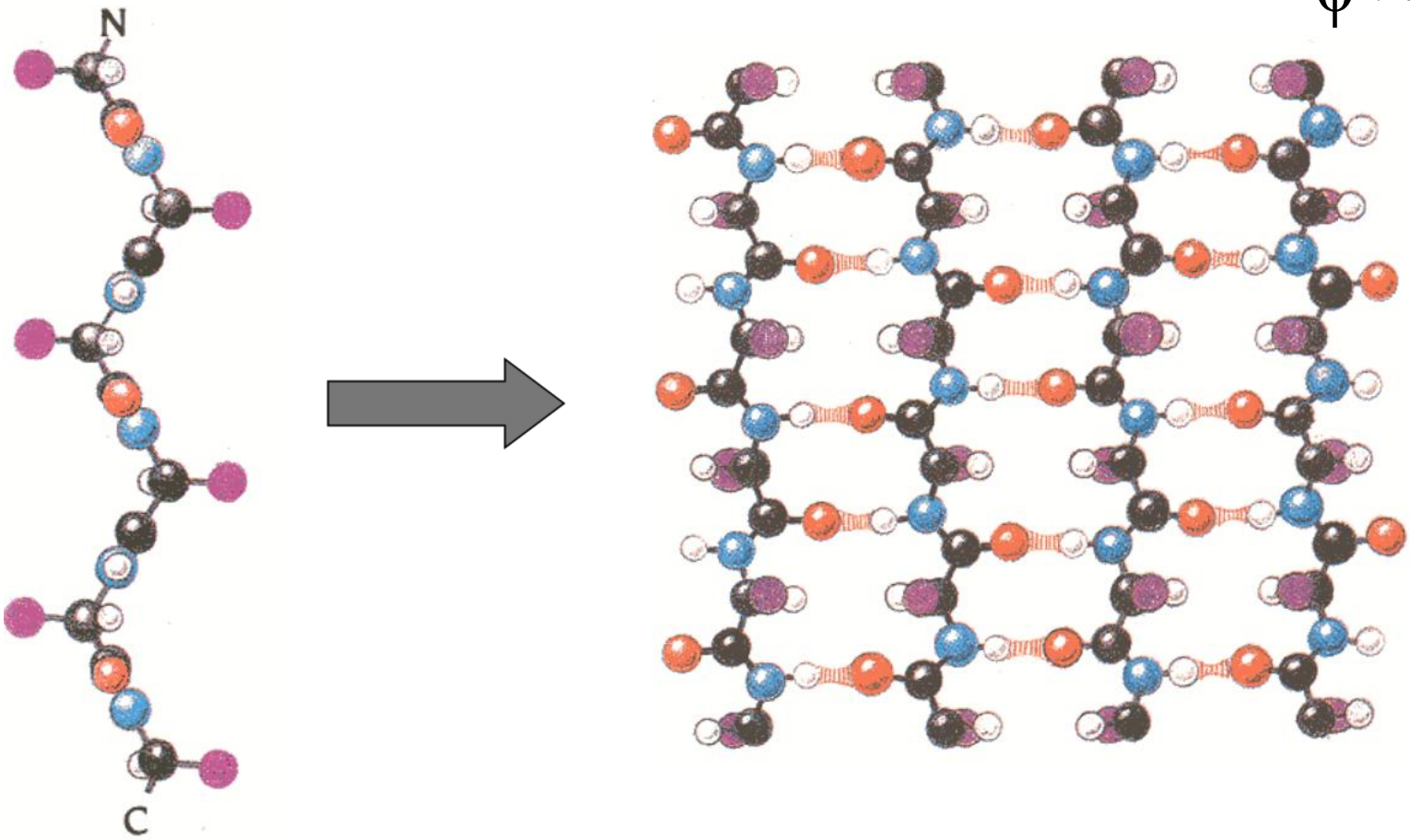


Alcohol dehydrogenase

The beta strand (& sheet)

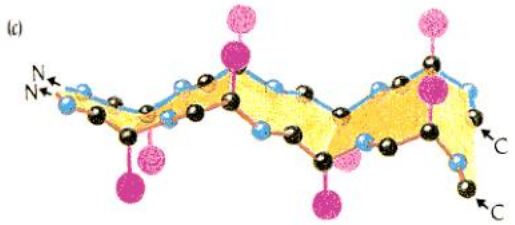
$\varphi \approx -135°$

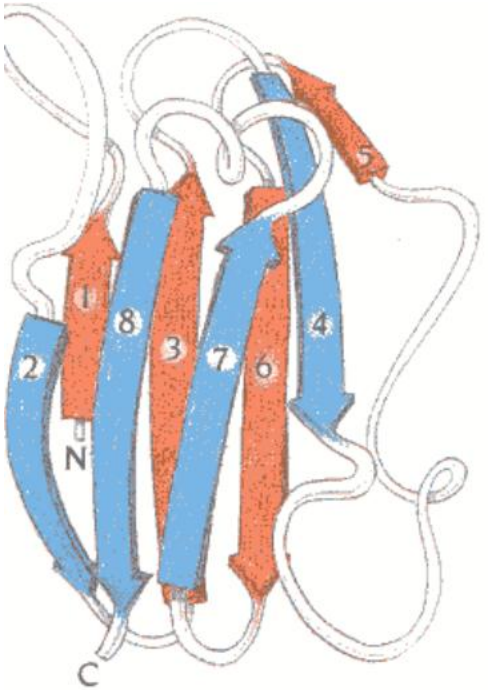
$\psi \approx +135°$

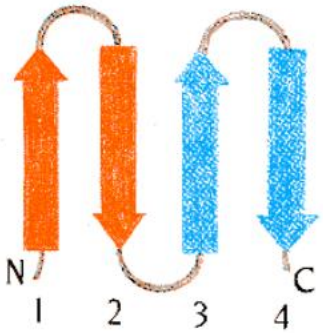


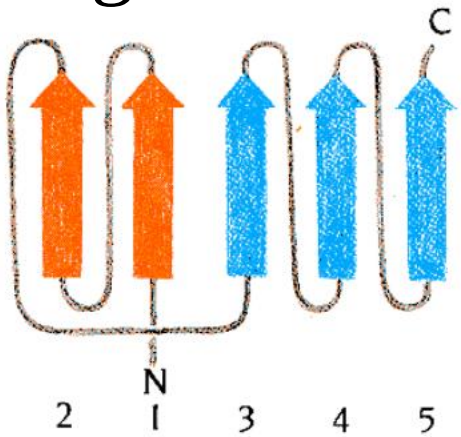
Properties of beta sheets

- Formed of stretches of 5-10 residues in extended conformation
- *Pleated* – each Cα a bit above or below the previous
- *Parallel/aniparallel*, contiguous/non-contiguous





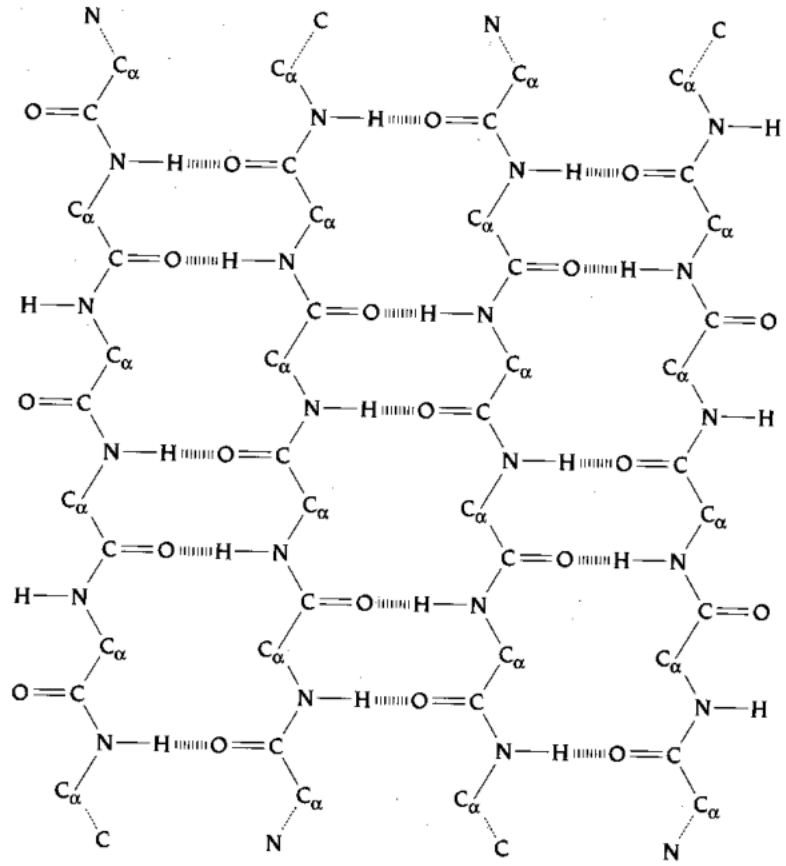




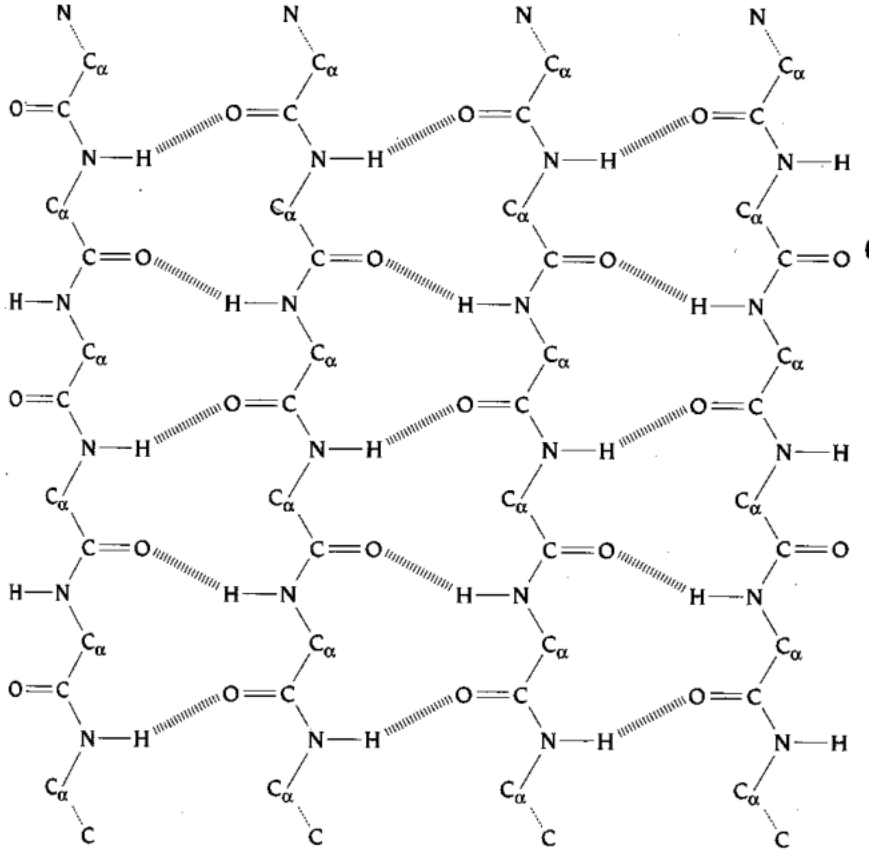
Parallel and anti-parallel β-sheets

- Anti-parallel is slightly energetically favored

Anti-parallel

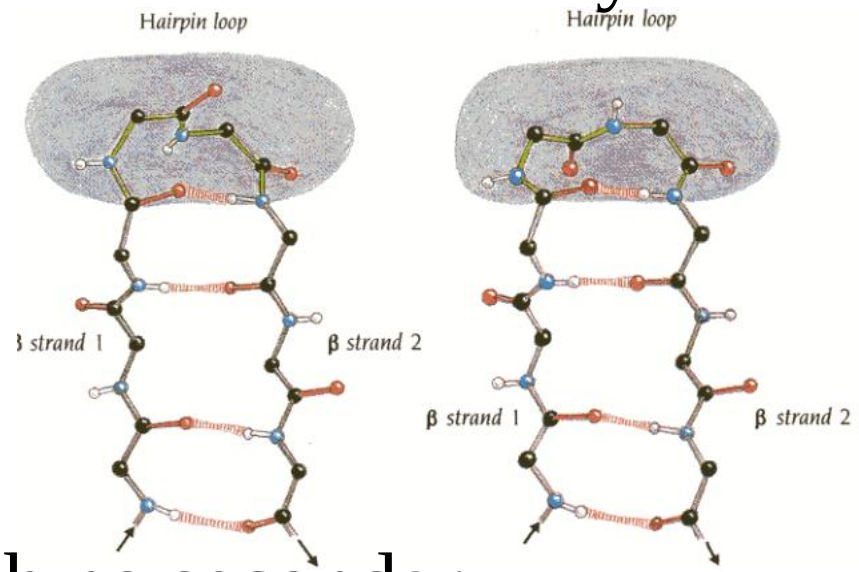


Parallel



Turns and Loops

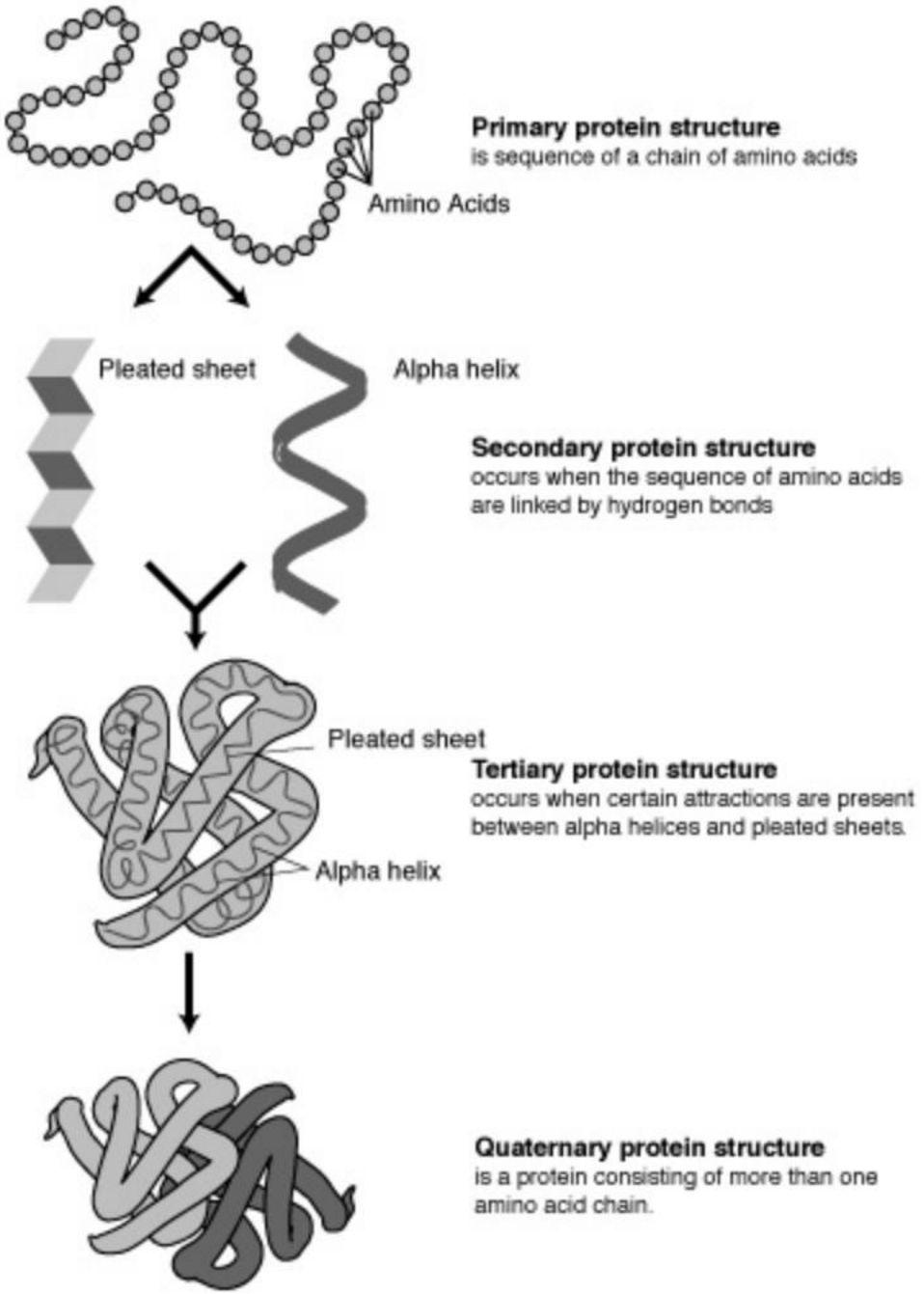
- Secondary structure elements are connected by regions of *turns* and *loops*
- Turns – short regions of non-α, non-β conformation



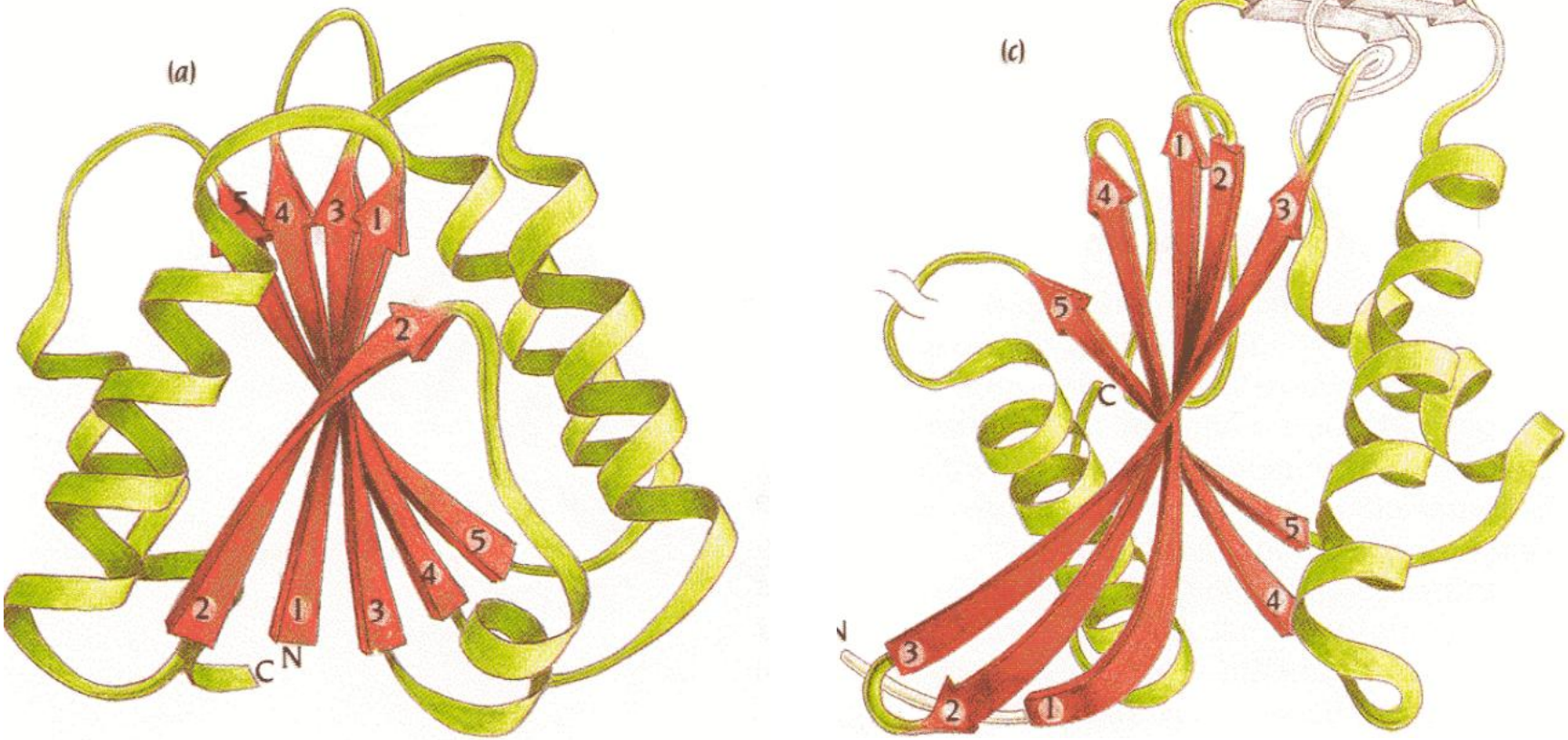
- Loops – larger stretches with no secondary structure. Often disordered.
  - "Random coil"
  - Sequences vary much more than secondary structure regions

Levels of Protein Structure

- Secondary structure elements combine to form tertiary structure
- Quaternary structure occurs in multienzyme complexes
  - Many proteins are active only as homodimers, homotetramers, etc.

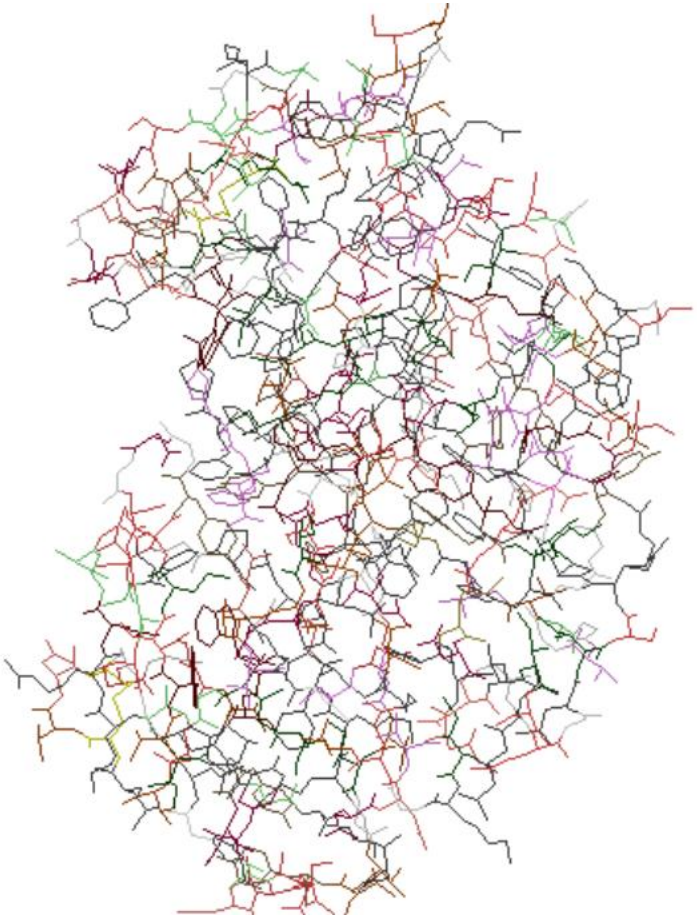


Protein Structure Examples

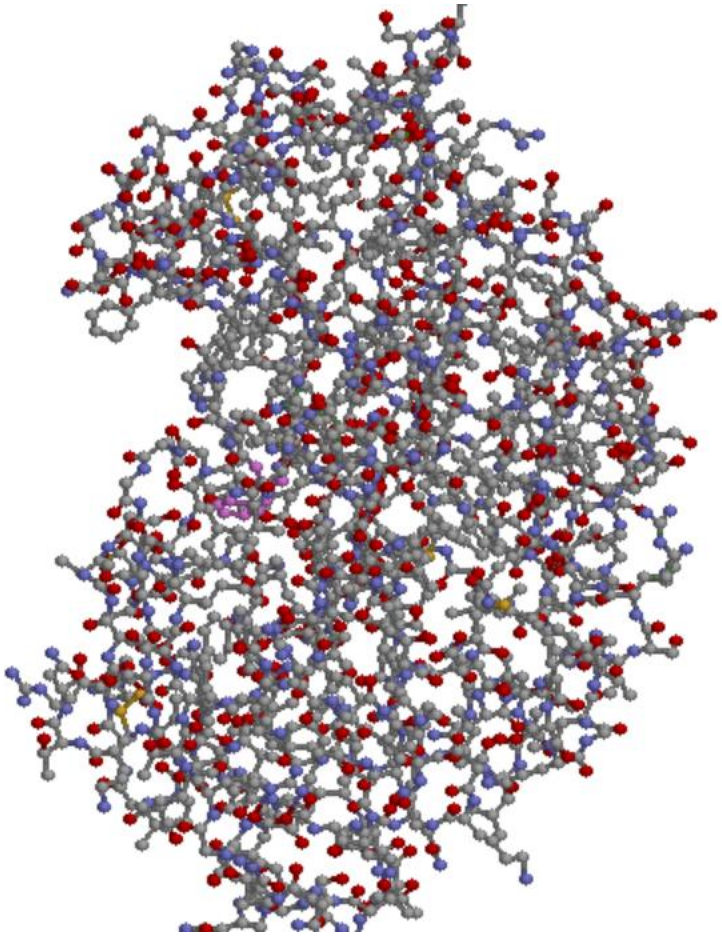


Views of a protein

Wireframe

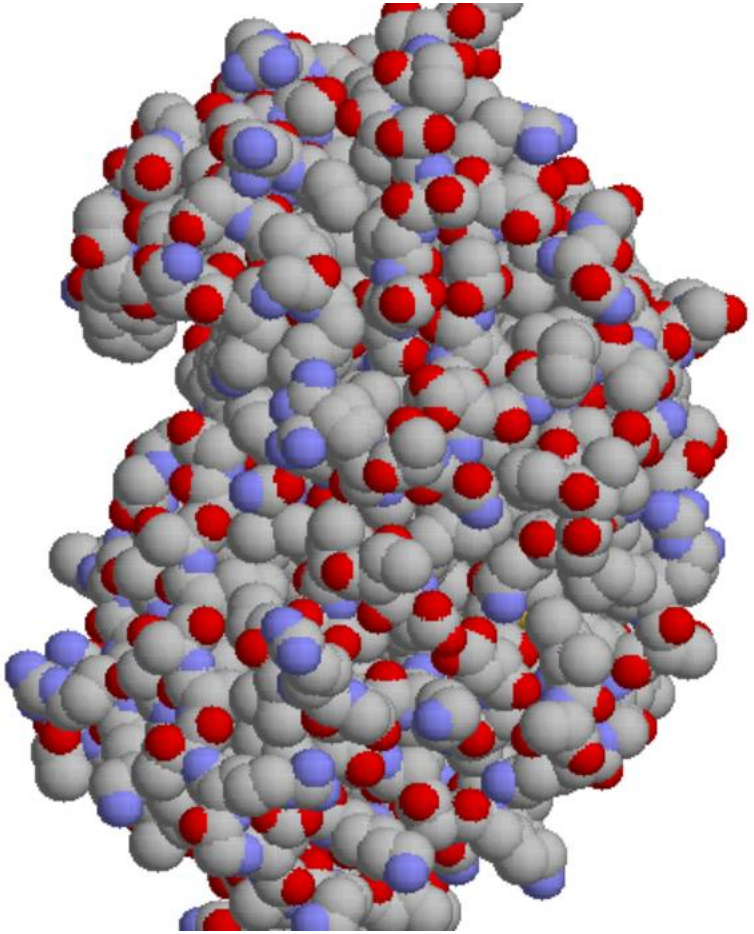


Ball and stick

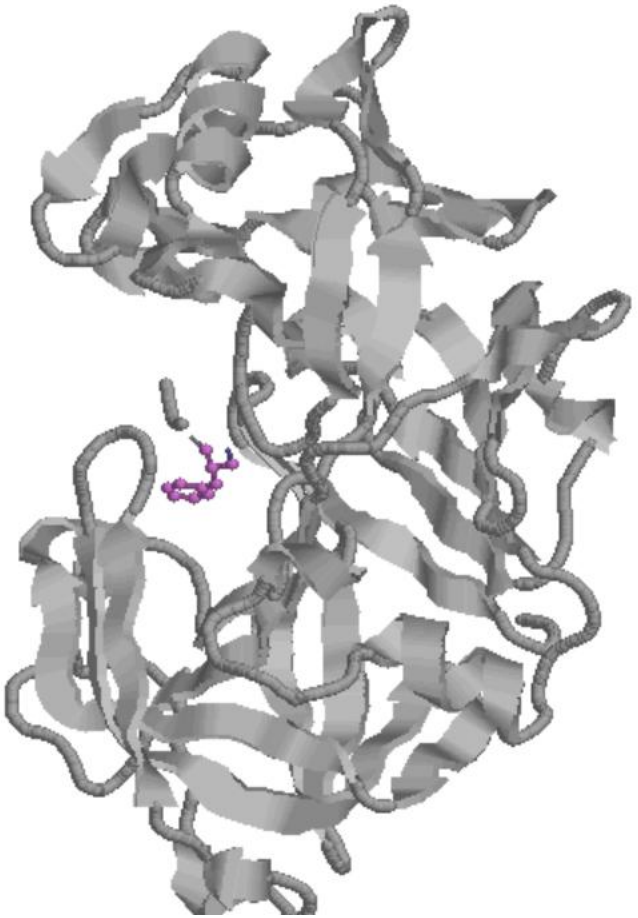


Views of a protein

Spacefill



Cartoon



CPK colors

Carbon = green, black, or grey

Nitrogen = blue

Oxygen = red

Sulfur = yellow

Hydrogen = white