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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
- Vitellogenin: 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
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: \( \text{N–C}_\alpha–\text{C} \cdots \text{N–C}_\alpha–\text{C} \)
  \[ \text{O} \quad \text{O} \]

- 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

Proline severely limits allowable conformations!
The Charged Amino Acids

- Asp, Aspartic acid
- Glu, Glutamic acid
- Lys, Lysine
- Arg, Arginine
The Polar Amino Acids

- Ser, Serine
- Thr, Threonine
- Tyr, Tyrosine
- Cys, Cysteine
- Asn, Asparagine
- Gln, Glutamine
More Polar Amino Acids

And then there’s...

His, Histidine

Gly, Glycine

Trp, Tryptophan
Planarity of the peptide bond

Phi (\(\phi\)) – the angle of rotation about the N-C\(\alpha\) bond.

Psi (\(\psi\)) – the angle of rotation about the C\(\alpha\)-C bond.

The planar bond angles and bond lengths are fixed.

Protein Structure and Function
**Phi and psi**

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

- 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

$\phi \approx \psi \approx -60^\circ$
Properties of the alpha helix

- $\phi \approx \psi \approx -60^\circ$
- **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
The beta strand (& sheet)

$\phi \approx -135^\circ$

$\psi \approx +135^\circ$
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/antiparallel*, 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