

Protein Structure

Stryer Short Course
Chapter 4

Peptide bonds

- Amide bond
- Primary structure
- N- and C-terminus
- Condensation and hydrolysis

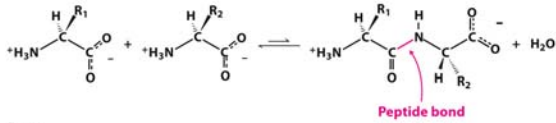


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Polypeptides

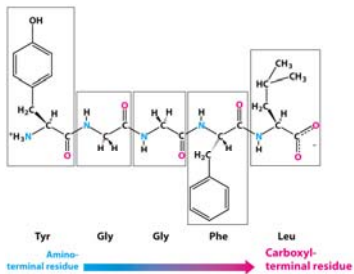


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Drawing Peptides

- Sidechains
- Stereochemistry
- Ionization states
- Example: Draw the peptide AHSCVE at pH 8.
- Steps
 - Backbone
 - Stereochemistry
 - Sidechains
 - Check ionization

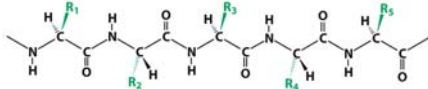
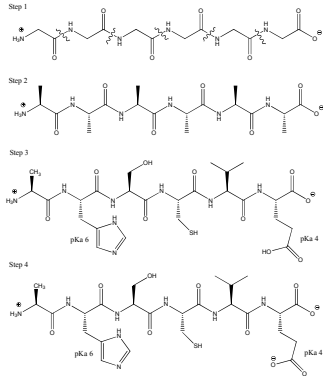


Figure 4.3
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Example: Draw the peptide AHSCVE at pH 8.



Disulfide bond formation

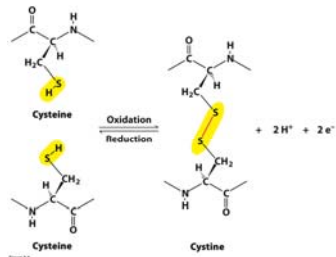
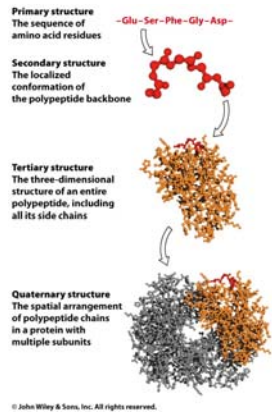


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Primary Structure

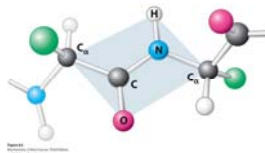
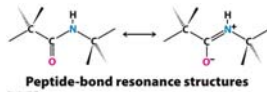
- Protein defined by unique primary sequence
- Structure defined by primary sequence
- Function dictated by structure
- Basis of understanding mutation





Basis of Secondary Structure

- Polarity
- Rigidity
- Planarity

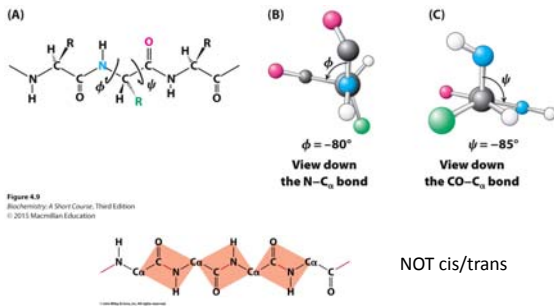


Cis and Trans Peptide Bonds

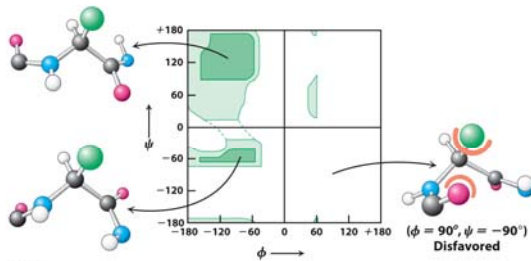


- Double bond character
- Slowly interchangeable
- Trans heavily favored—steric interactions

Conformational Constraint



Ramachandran Plots



Alpha Helix

- Right handed
- Polarity
- n and $n + 4$
- Gly and Pro

Figure 4.11
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Figure 4.12
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Helical Wheel

- The sequence of a domain of the gp160 protein(HIV) is shown below using one-letter codes for the amino acids. Plot this sequence on the helical wheel. What do you notice about the amino acid residues on either side of the wheel?

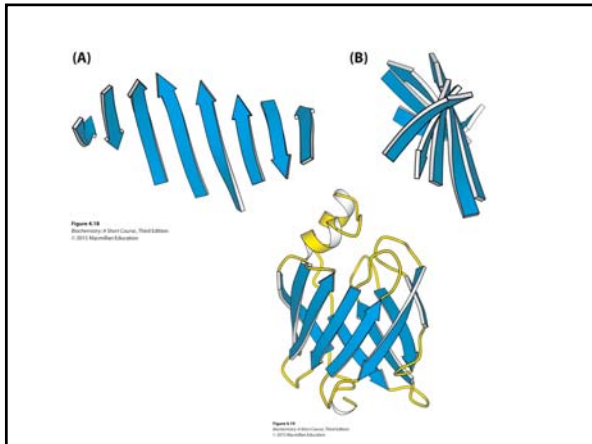
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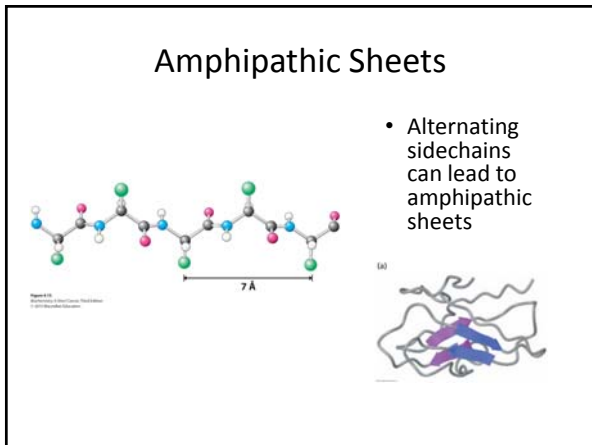
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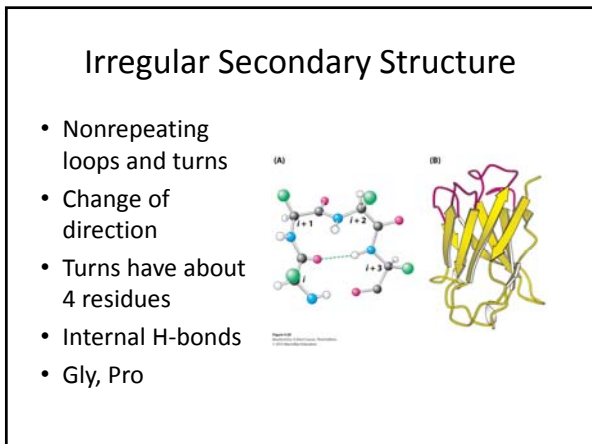
Beta Sheets

- Parallel
- Antiparallel
- mixed

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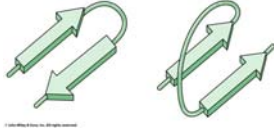






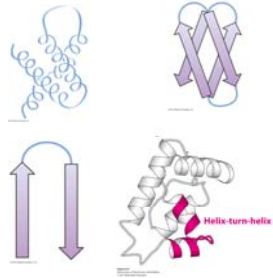
Tertiary Structure

- Too many shapes to memorize
- But not an infinite number of possibilities
- Take away the ability to read a paper
 - Discussions of **motifs** and why important
 - Discussion of **domains** and why important



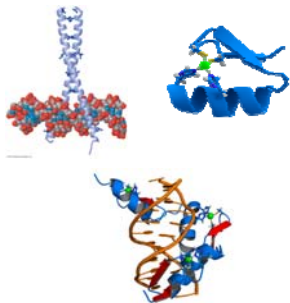
Motifs (Super Secondary Structure)

- Recognizable combinations of helices, loops, and sheets
- Match
 - Helix-turn-helix
 - Helix bundle
 - Hairpin
 - β -sandwich



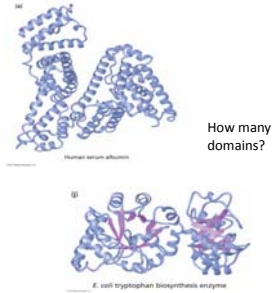
Studying Motifs

- Some Motifs are highly studied
- Know the lingo
 - Leucine zipper
 - Zinc finger
- Often have recurring applications

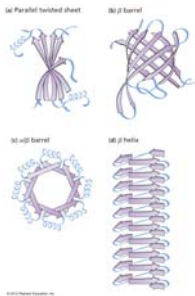


Structural and Functional Domains

- Discrete, independently folded unit (may maintain shape when cleaved on loop)
- May have separate activities: "ATP binding domain" or "catalytic domain"
- Similar activity = similar structure across many proteins
- Binding pockets at interfaces

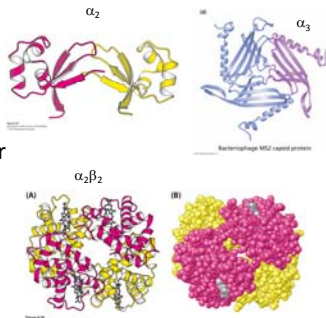


Common Domains



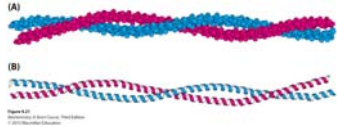
Quaternary Structure

- Multiple subunits: Oligomers
- Homodimer, heterotetramer
- Advantages
 - Economy
 - Stability
 - regulation



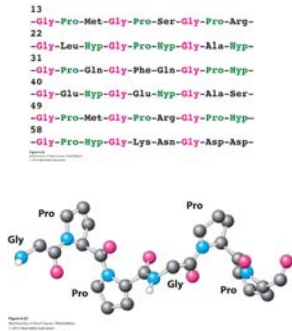
Protein Structure

- Fibrous Proteins
 - Keratin—coiled coil
 - Collagen—triple helix
- Globular Proteins
 - Myoglobin



Collagen

- Repeating Gly and Pro
- Hyp: hydroxyproline
 - Oxidized form
 - Requires vitamin C
 - Scurvy



Collagen

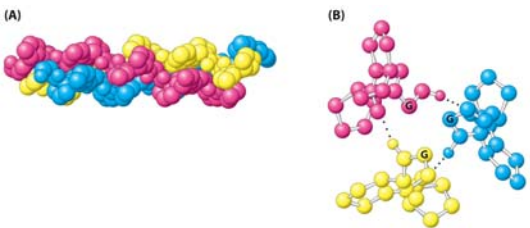


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Myoglobin

- Globular Protein
- Hydrophobic effect
- Helix bundle
- Polar loops
- Nonpolar core

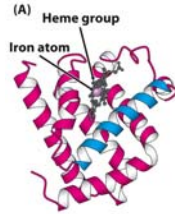


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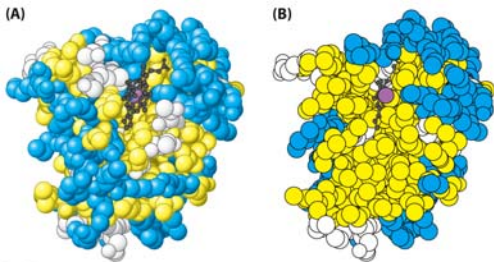


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Protein Folding

- Native vs denatured states
- ΔG might be 40 kJ/mol for small protein (about 2 H-bonds)
- Classic Anfinsen experiments show folding info contained in primary sequence (in many cases)

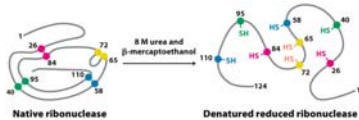
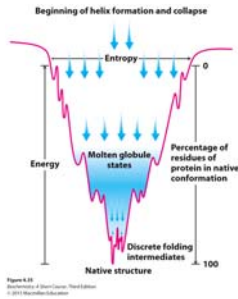


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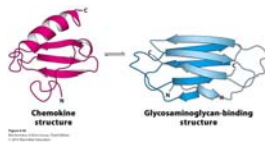
Thermodynamics and Kinetics

- Levinthal's paradox: not random sampling of all possible conformations
- Energy funnel
- Series of irreversible steps
- Entropy traps



More than one fold

- Traditionally, one protein = one fold
- Intrinsically Unstructured Proteins (IUPs) are more common than originally thought
- Metamorphic proteins
 - Cytokine with equilibrium of two structures with necessary function



Misfolding Pathology

- Amyloidoses
 - Alzheimer, Parkinson, Huntington, prion
- Formation of amyloid fibers
 - The less stable protein form accumulates into a nucleus, which grows to a fibril
 - Aggregations cause damage—oxidation??
- Mad Cow Disease: prions as the infectious agent

