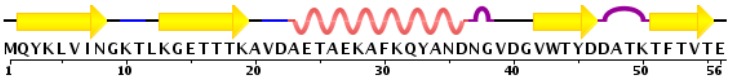
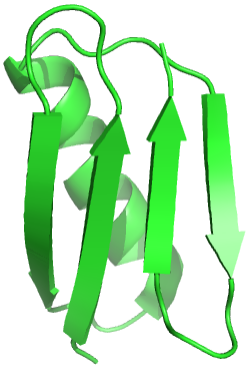
Protein Structure

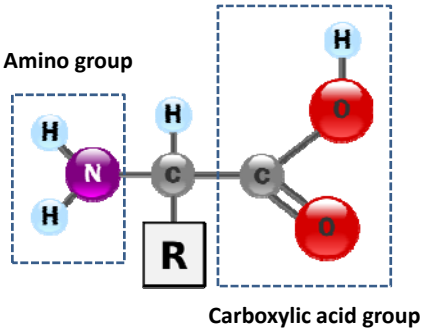
Biochemistry Boot Camp
Session #1
Ailin Wang
aw1229@msstate.edu



- Amino Acids



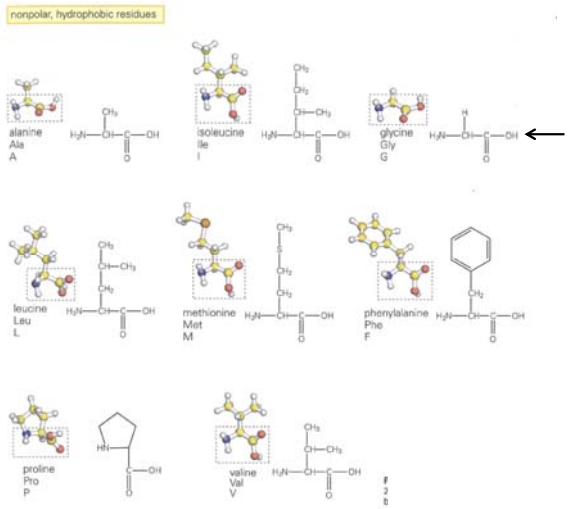
Cartoon Model



PDB code:2OED

Nonpolar Amino Acids

(side chain is uncharged at neutral pH, cannot participate in hydrogen bonding)



Beware! Incorrect Ionization!

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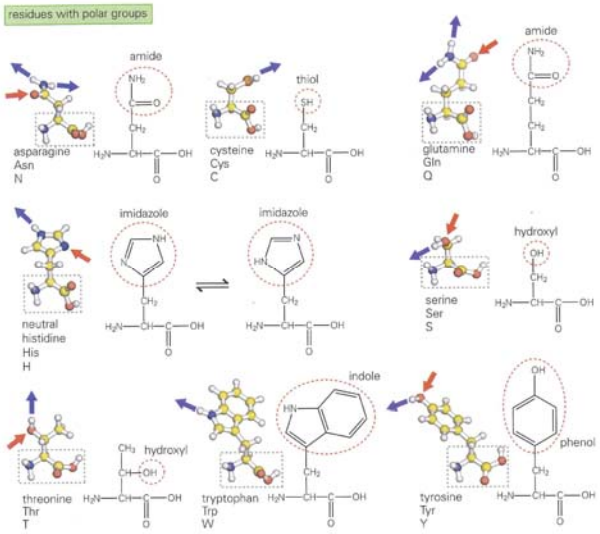
Polar Amino Acids

(side chain is uncharged at neutral pH, can donate or accept hydrogen bonds)



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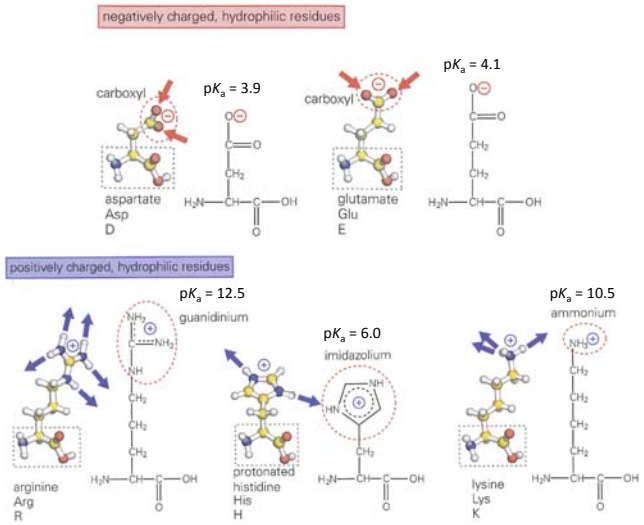
Ionizable Amino Acids

(with typical side-chain pK_a values, charged at neutral pH)



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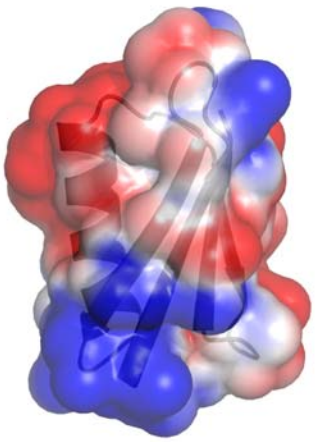
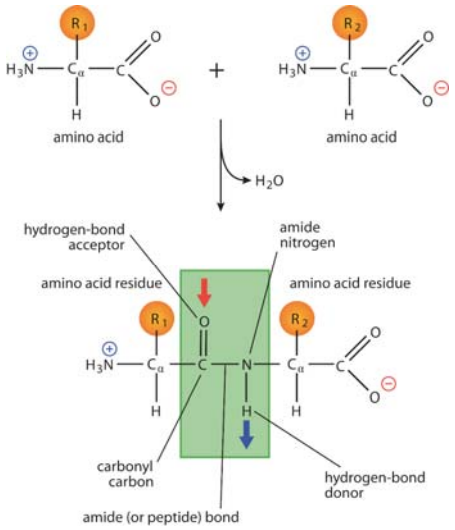
Electrostatic surface



Red – negative charge

Blue – positive charge

Making Peptide Bonds: Condensation



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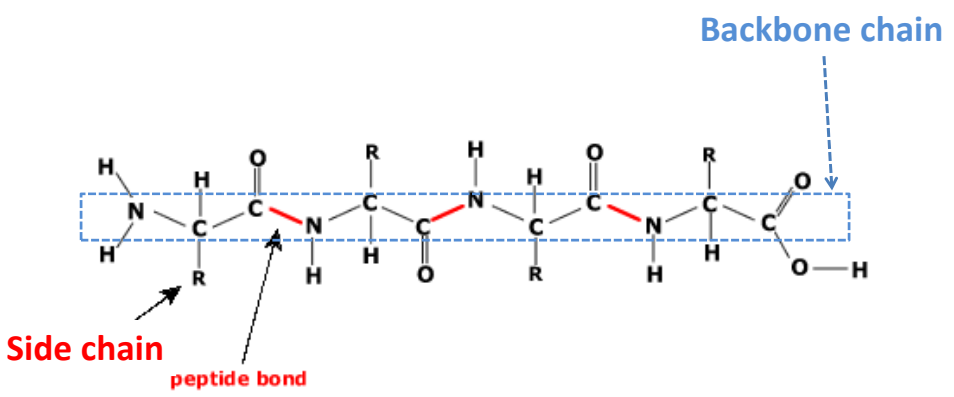
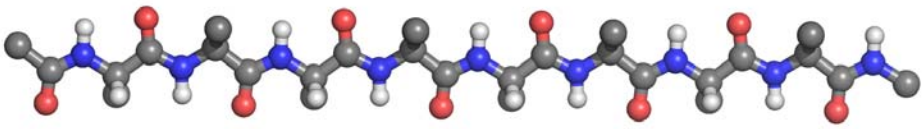
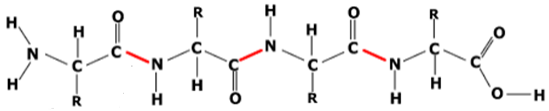


The Protein "Backbone"



Blue: N
Grey: C_{α}, C_{COOH}
Red: O
White: H_{α}, H_{NH}



- Directionality: NT → CT is convention
- Atom names describe position in chain
- Side chains are added to the backbone

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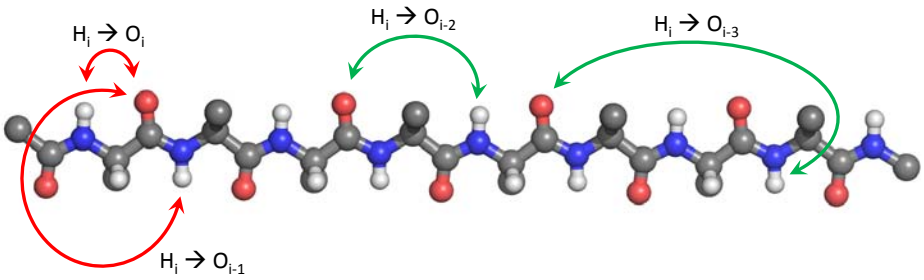
Backbone Hydrogen Bonding



- Non-repeating backbone patterns:
  - **Too much strain:** $H_i \rightarrow O_i$ and $H_i \rightarrow O_{i\pm1}$ hydrogen bonds
  - **Rare, but possible:** $H_i \rightarrow O_{i-2}$ (Gamma turns)
  - **Frequently observed:** $H_i \rightarrow O_{i-3}$ (Beta turns)

H-bond: H-O, N, F

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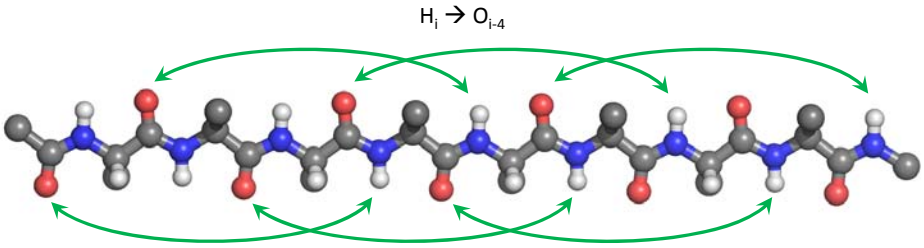
Backbone Hydrogen Bonding



- The Alpha Helix Can be Repeated
  - $H_i \rightarrow O_{i-4}$ (Gamma turns)
  - Average ϕ is = -60°, Average ψ is -40°

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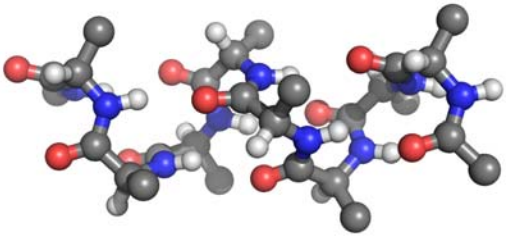
A (Right-Handed) Alpha Helix



- Download helix.pdb from the course website for a model you can examine in PyMOL
- Notice that helix ends have unsatisfied H-bonds

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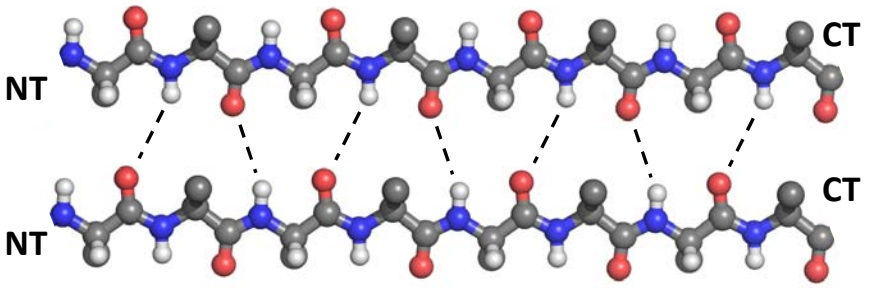
Backbone Hydrogen Bonding



- Beta sheets are made of beta strands
  - No specified hydrogen bonding formula
  - Sheets can form between distant sets of residues
  - **Shown:** Parallel beta sheet

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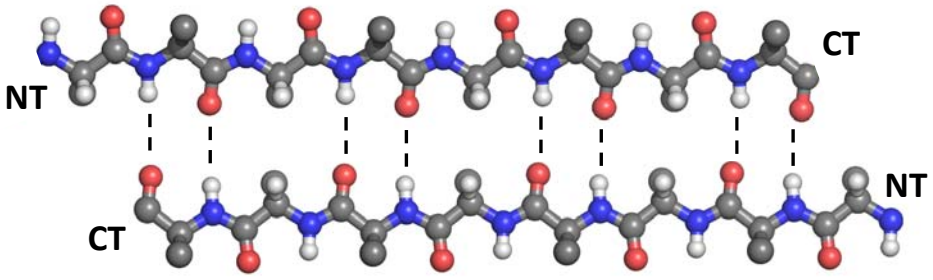
Backbone Hydrogen Bonding



- Beta sheets are made of beta strands
  - No specified hydrogen bonding formula
  - Average ϕ is = -120°, Average ψ is 120° (with large variation)
  - Sheets can form between distant sets of residues
  - **Shown:** Antiparallel beta sheet

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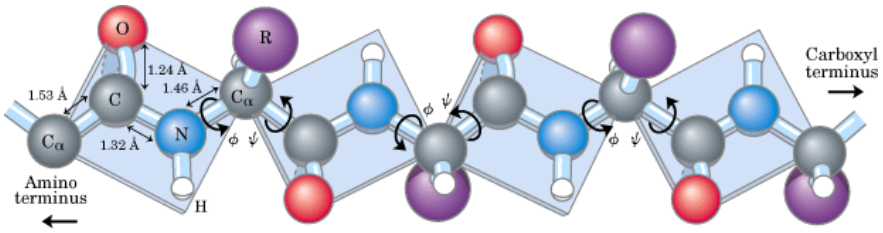
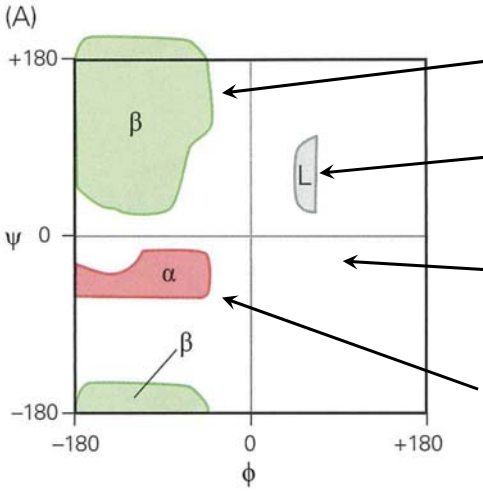
Making Sense of the Backbone



The Ramachandran Plot:

Sterically-allowed ϕ and ψ



Beta strand region

Left-handed alpha helix region
(Rare, but short helices do happen.)

White regions are "disallowed"
because of steric clash (atoms bump)

Alpha helix region

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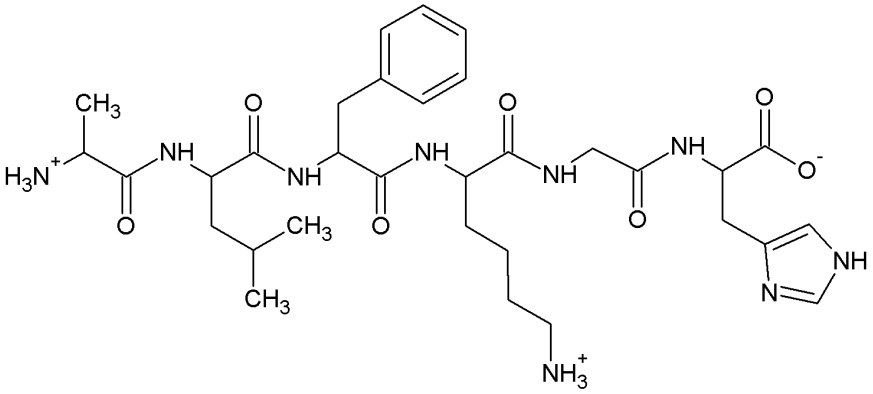
Primary Structure



Think: Sequence of amino acids

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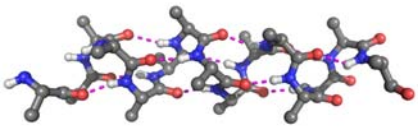
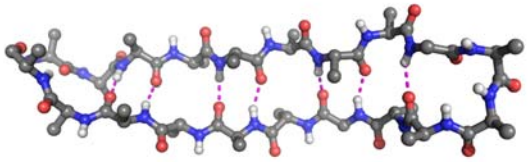
Secondary Structure



α Helices

β Strands/Turns



Think: Backbone hydrogen bonding

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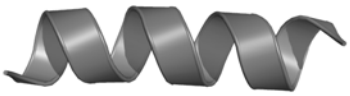
Secondary Structure



α Helices

β Strands/Turns

Think: Backbone hydrogen bonding

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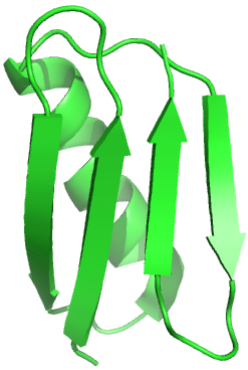
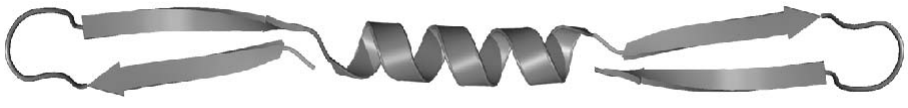
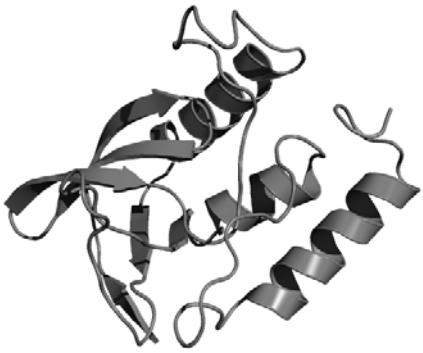


OR ?



Tertiary Structure



Think: Three-dimensional coordinates

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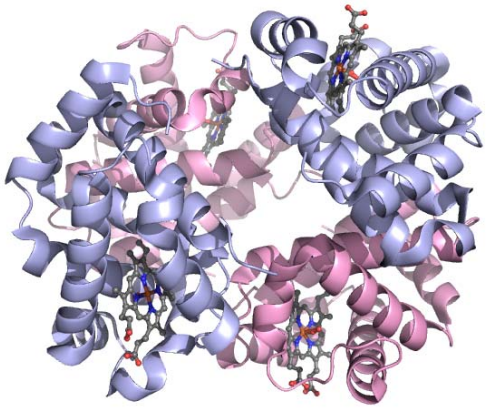
Quaternary Structure



Think: Complexes of multiple proteins

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Summary

- Proteins are chemical chains, made up of 20 different amino acids
- The chemical structure of the backbone has consequences: helices, sheets, and turns
- Protein structure is classified into a four-level hierarchy