

Protein Structure

Biochemistry Boot Camp 2019
Session #1
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Nonpolar Amino Acids

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

nonpolar, hydrophobic residues

Beware!
Incorrect
ionization!

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Different representations of proteins

MQYKLVINGKTLKGETTTKAVDAETA EKAFKQYANDNGVDGVWYDDATKTFVT E

• Amino Acids

Alpha carbon (chiral carbon)
Amino group
Side chain (functional group)
Carboxylic acid group

Cartoon Model

PDB code:2OED

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Polar Amino Acids

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

residues with polar groups

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Ionizable Amino Acids

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

negatively charged, hydrophilic residues

$pK_s = 3.9$

carboxyl
aspartate
Asp
D

$pK_s = 4.1$

carboxyl
glutamate
Glu
E

positively charged, hydrophilic residues

$pK_s = 12.5$

guanidinium
arginine
Arg
R

$pK_s = 6.0$

imidazolium
protonated histidine
His
H

$pK_s = 10.5$

ammonium
lysine
Lys
K

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Making Peptide Bonds: Condensation

Molecules of Life, pp. 28

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Electrostatic surface

Neutral groove

Red – negative charge

Blue – positive charge

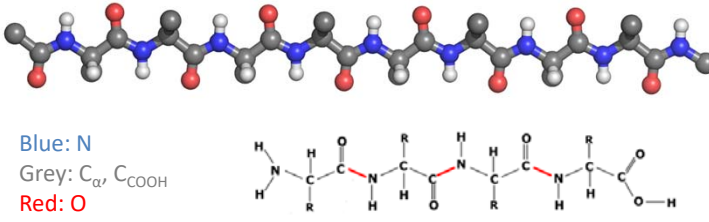
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Think and Discuss

What's the advantage to having twenty amino acids?

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The Protein "Backbone"



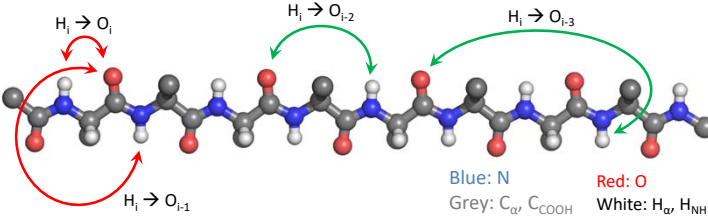
Blue: N
 Grey: C α , C $_{COOH}$
 Red: O
 White: H α , H $_{NH}$

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

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Backbone Hydrogen Bonding



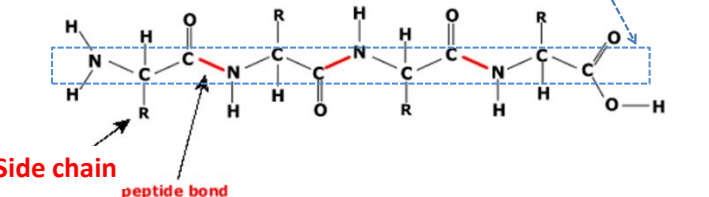
- Non-repeating backbone patterns:
 - Too much strain: H $_i \rightarrow O_i$ and H $_i \rightarrow O_{i\pm 1}$ hydrogen bonds
 - Rare, but possible: H $_i \rightarrow O_{i-2}$ (Gamma turns)
 - Frequently observed: H $_i \rightarrow O_{i-3}$ (Beta turns)

H-bond: H-O, N, F

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The Protein "Backbone"



Backbone chain

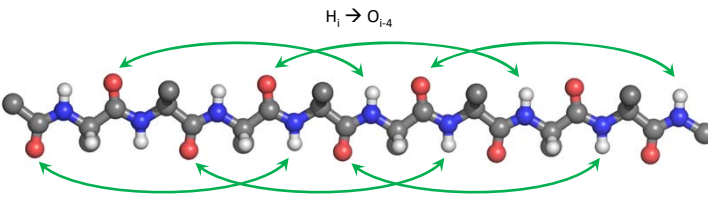
Side chain

peptide bond

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Backbone Hydrogen Bonding

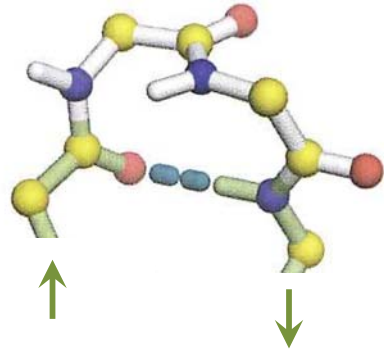


- The Alpha Helix Can be Repeated
 - H $_i \rightarrow O_{i-4}$ (Gamma turns)
 - Average ϕ is -60° , Average ψ is -40°

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Beta Turns Reverse the Direction of the Backbone

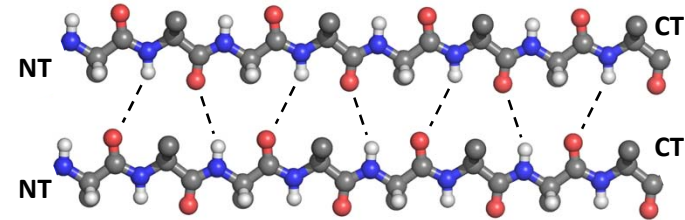


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Backbone Hydrogen Bonding

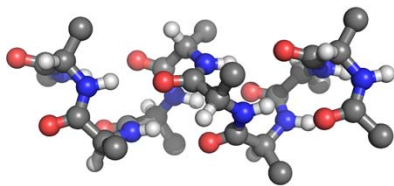


- Beta sheets are made of beta strands
 - No specified hydrogen bonding formula
 - Sheets can form between distant sets of residues
 - **Shown:** Parallel beta sheet

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A (Right-Handed) Alpha Helix



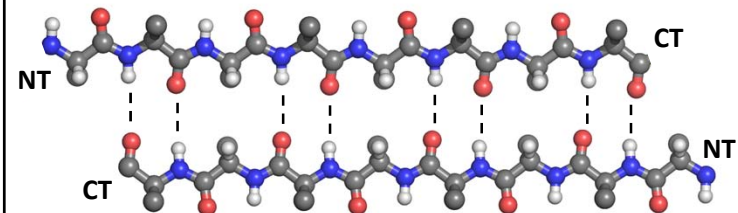
- Download helix.pdb from the course website for a model you can examine in PyMOL
- Notice that helix ends have unsatisfied H-bonds

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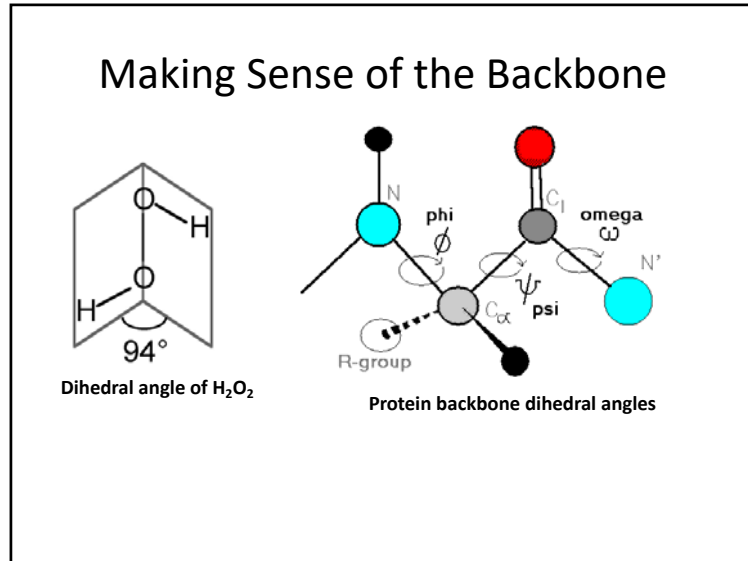
Backbone Hydrogen Bonding



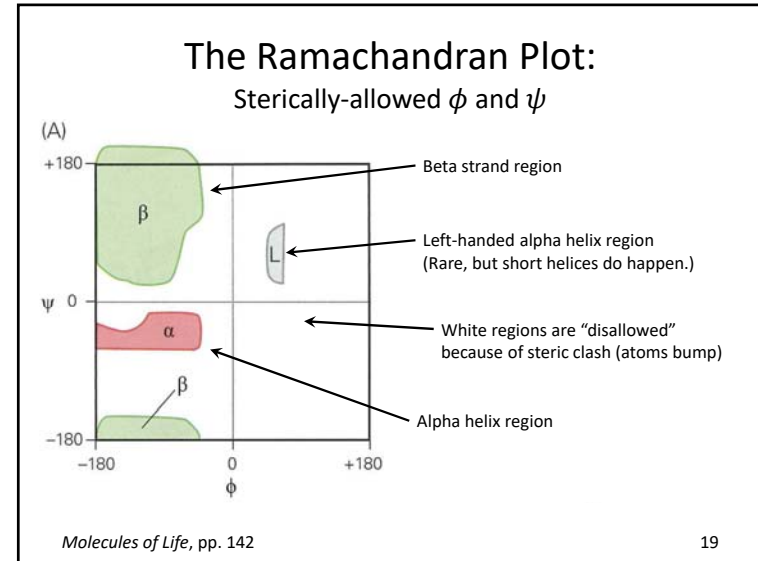
- Beta sheets are made of beta strands
 - No specified hydrogen bonding formula
 - Average ϕ is -120° , Average ψ is 120° (with large variation)
 - Sheets can form between distant sets of residues
 - **Shown:** Antiparallel beta sheet

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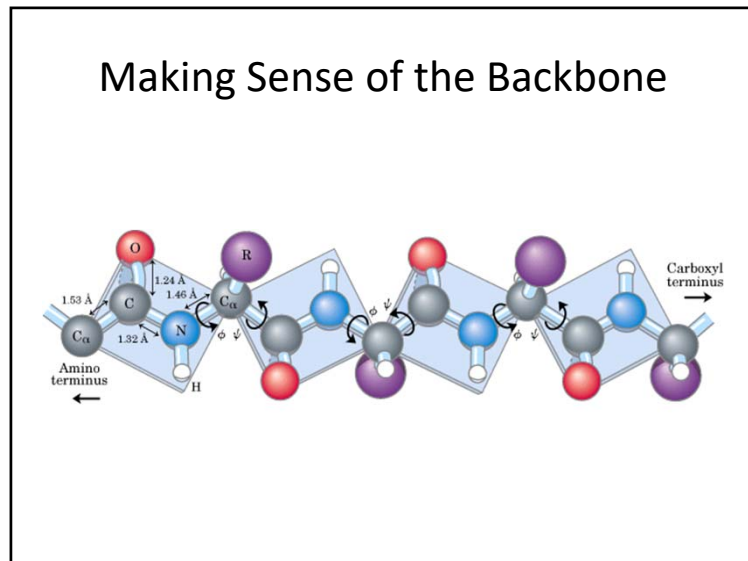


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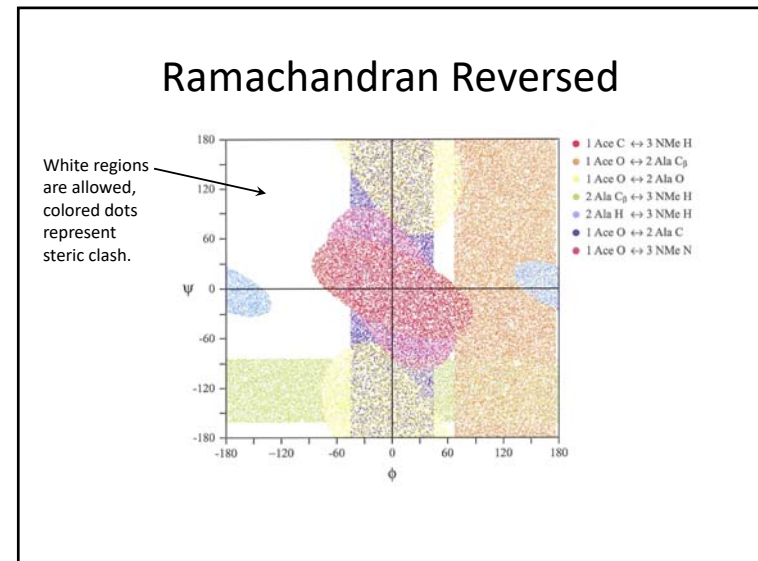


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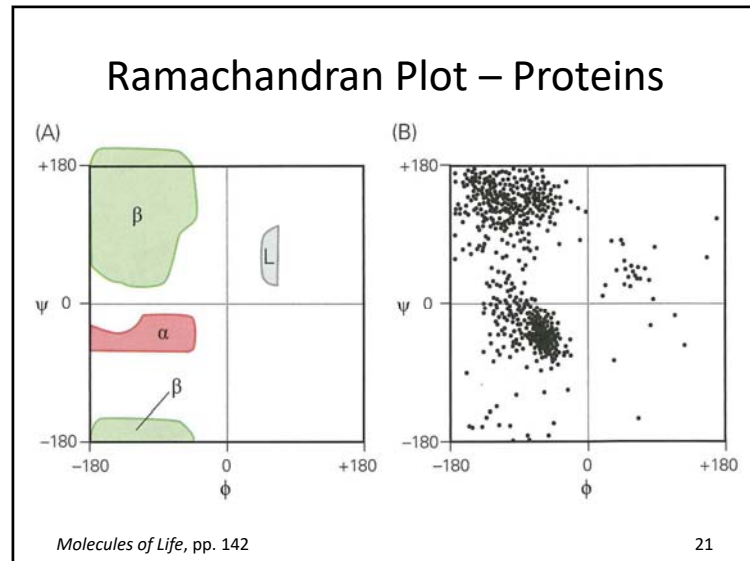
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Hierarchy of Structure

- First proposed by Linderstrøm-Lang

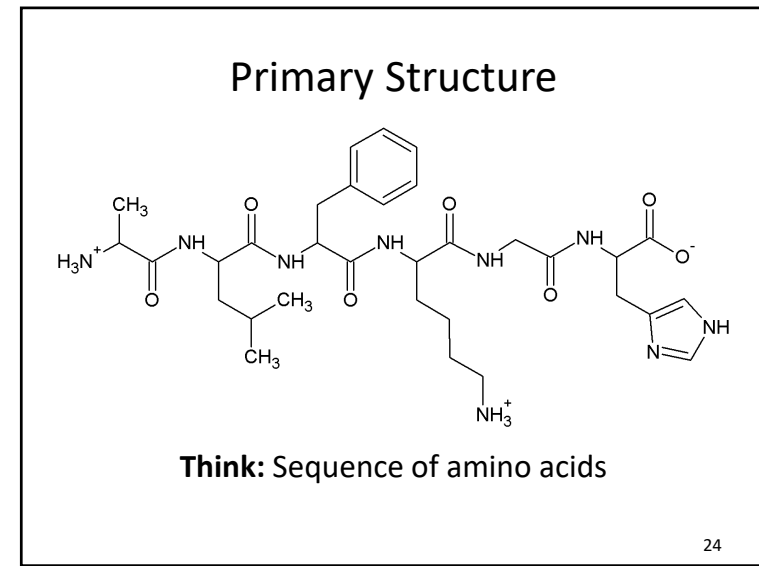
Sources: <http://www.biokemi.org/biozoom/issues/488/articles/1910>
http://en.wikipedia.org/wiki/Carlsberg_Laboratory

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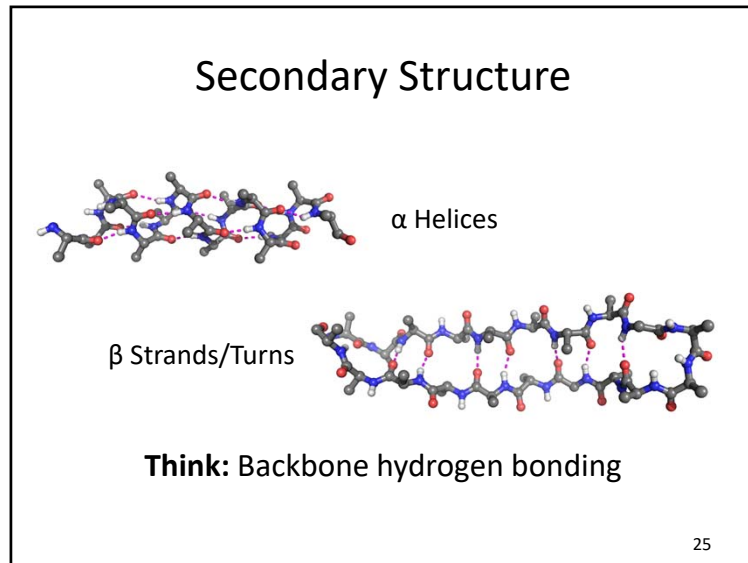
Think and Discuss

Why might you see violations to the Ramachandran plot?

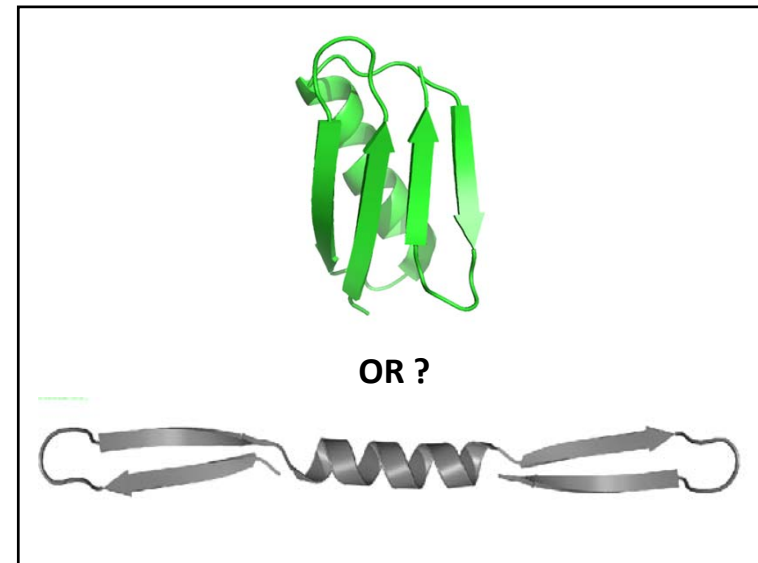
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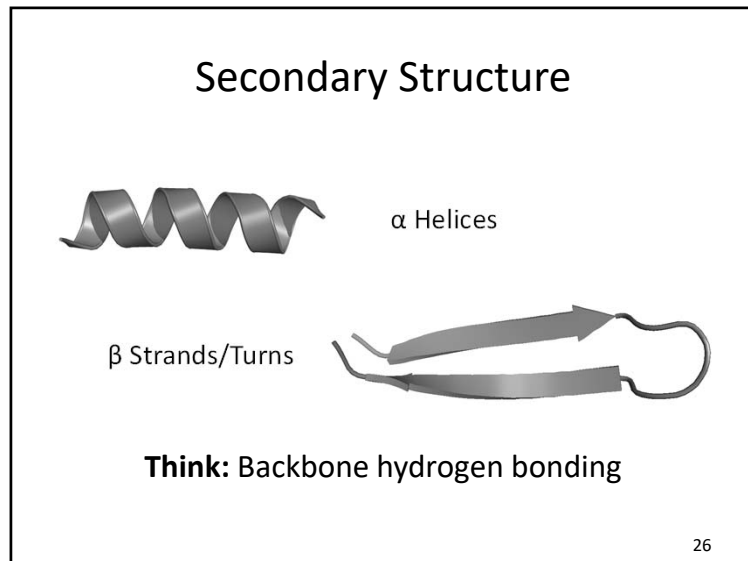
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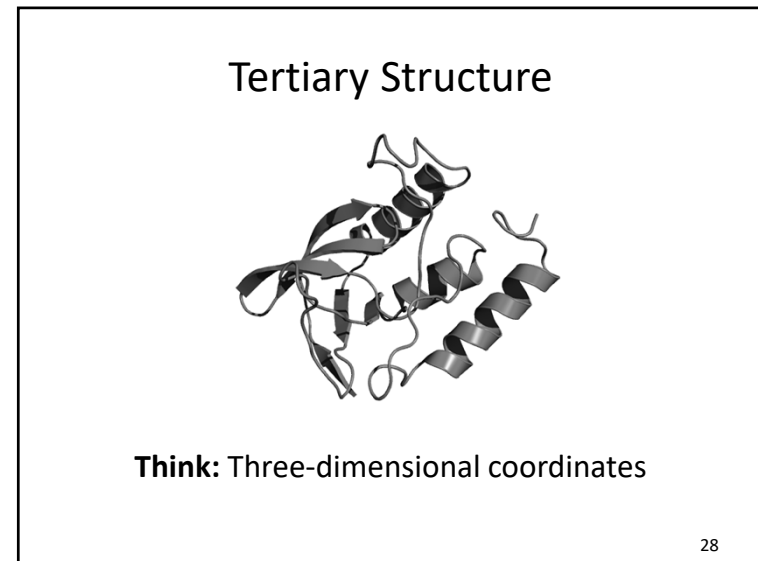
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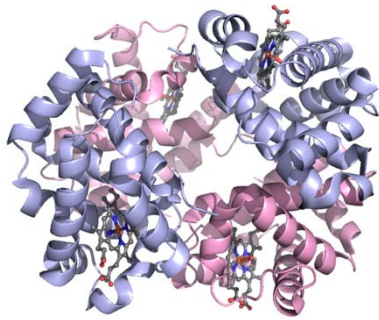


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Quaternary Structure



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

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Think and Discuss

Does it make sense to think about one type of structure being more important than another?

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