

PRIMARY AND SECONDARY STRUCTURE

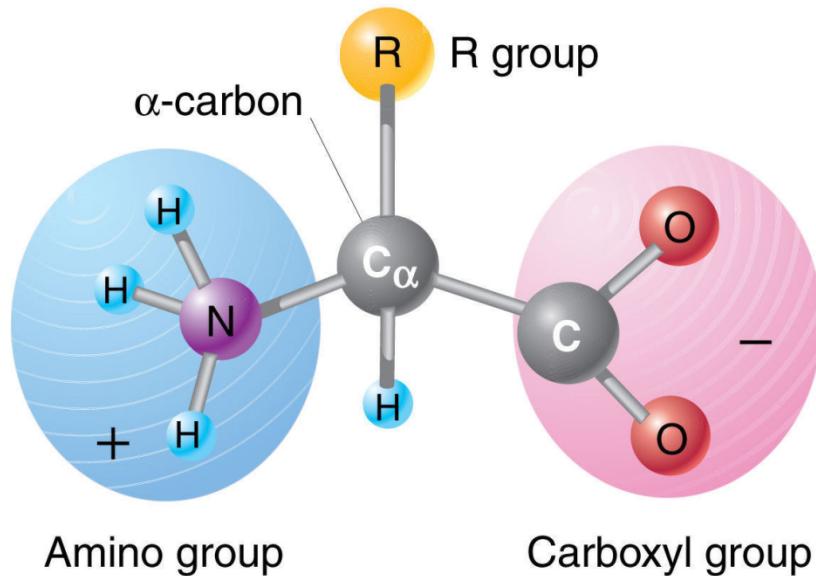
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SUSTC

Primary Structure

- Protein 3D structure depends on its amino acid sequence.



Amino Acid



- Refresh your memory about amino acids in “Biochemistry” course
 - Hydrophobic
 - Hydrophilic
 - Charged
 - ...

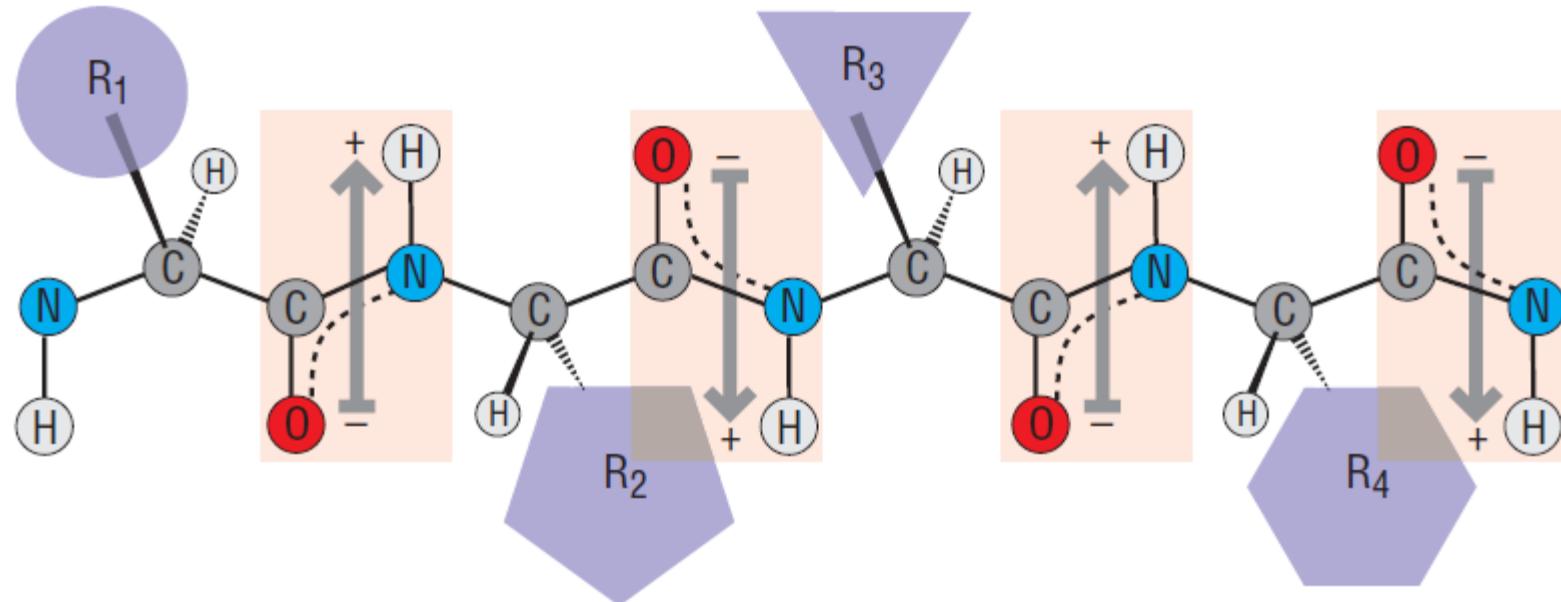
- The **chemical characters** of the amino-acid **side chains** have important consequences for the way they participate in the **folding and functions** of proteins

Similarity and Evolution

Table of the frequency with which one amino acid is replaced by others in amino-acid sequences of the same protein from different organisms

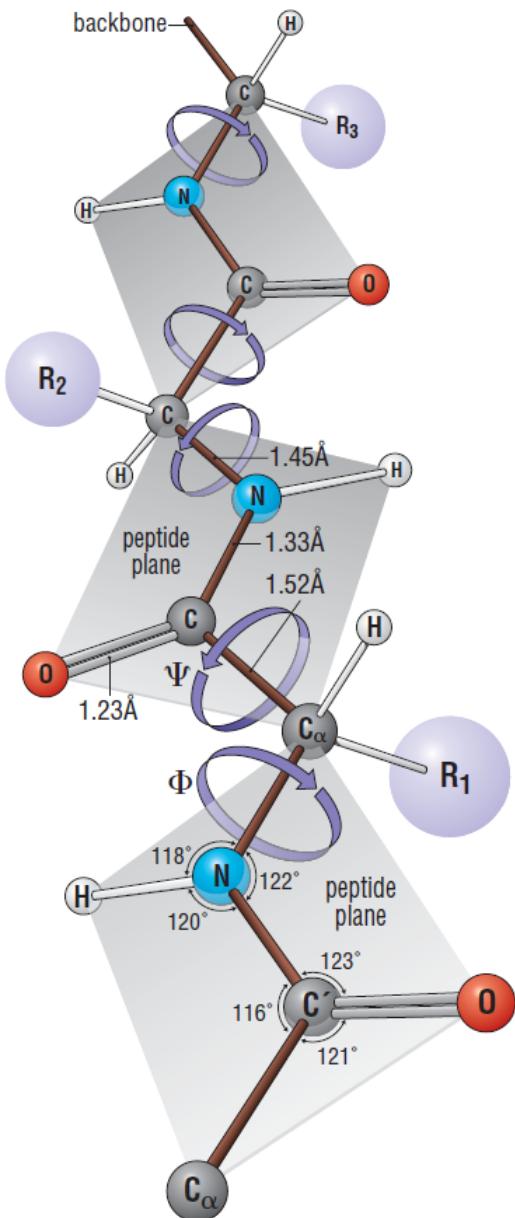
	Gly	Ala	Val	Leu	Ile	Met	Cys	Ser	Thr	Asn	Gln	Asp	Glu	Lys	Arg	His	Phe	Tyr	Trp	Pro
Gly																				
Ala	58																			
Val	10	37																		
Leu	2	10	30																	
Ile		7	66	25																
Met	1	3	8	21	6															
Cys	1	3	3		2															
Ser	45	77	4	3	2	2	12													
Thr	5	59	19	5	13	3	1	70												
Asn	16	11	1	4	4			43	17											
Gln	3	9	3	8	1	2		5	4	5										
Asp	16	15	2		1			10	6	53	8									
Glu	11	27	4	2	4	1		9	3	9	42	83								
Lys	6	6	2	4	4	9		17	20	32	15		10							
Arg	1	3	2	2	3	2	1	14	2	2	12	9		48						
His	1	2	3	4			1	3	1	23	24	4	2	2	10					
Phe	2	2	1	17	9	2		4	1	1						1	2			
Tyr		2	2	2	1		3	2	2	4				1	1		4	26		
Trp				1				2							3		1	1	1	
Pro	5	35	5	4	1		1	27	7	3	9	1	4	4	7	5	1			

Peptide



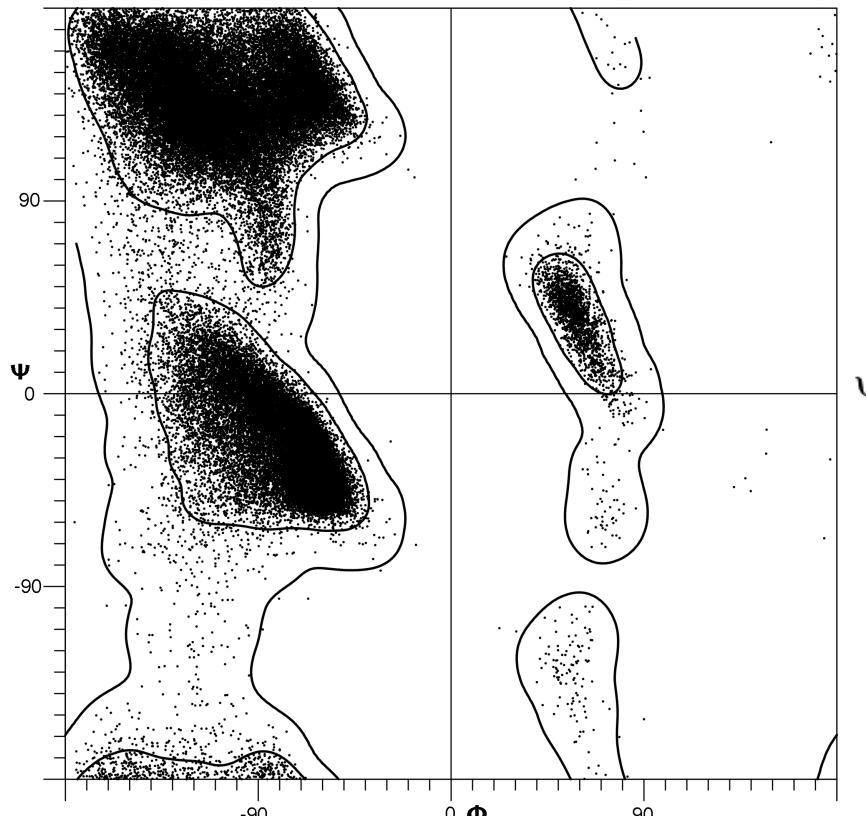
Peptide Conformation

- Bond lengths and bond angles
- Peptide plane
- Torsion angles
 - Phi / Φ
 - Psi / Ψ

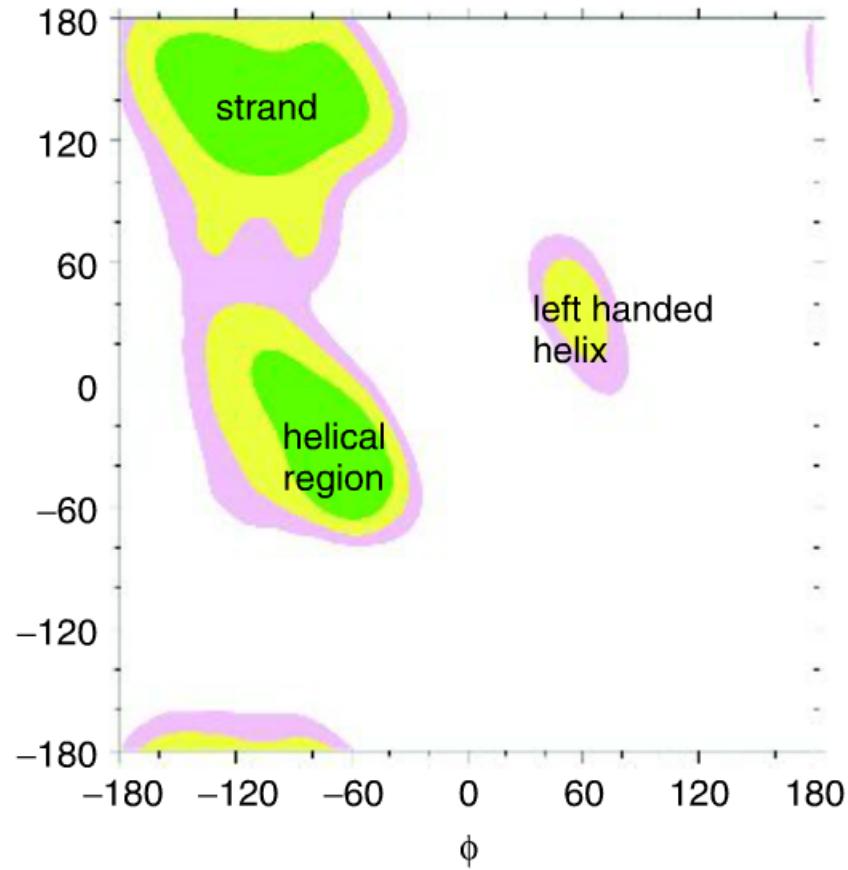


Torsion angles are not randomly distributed

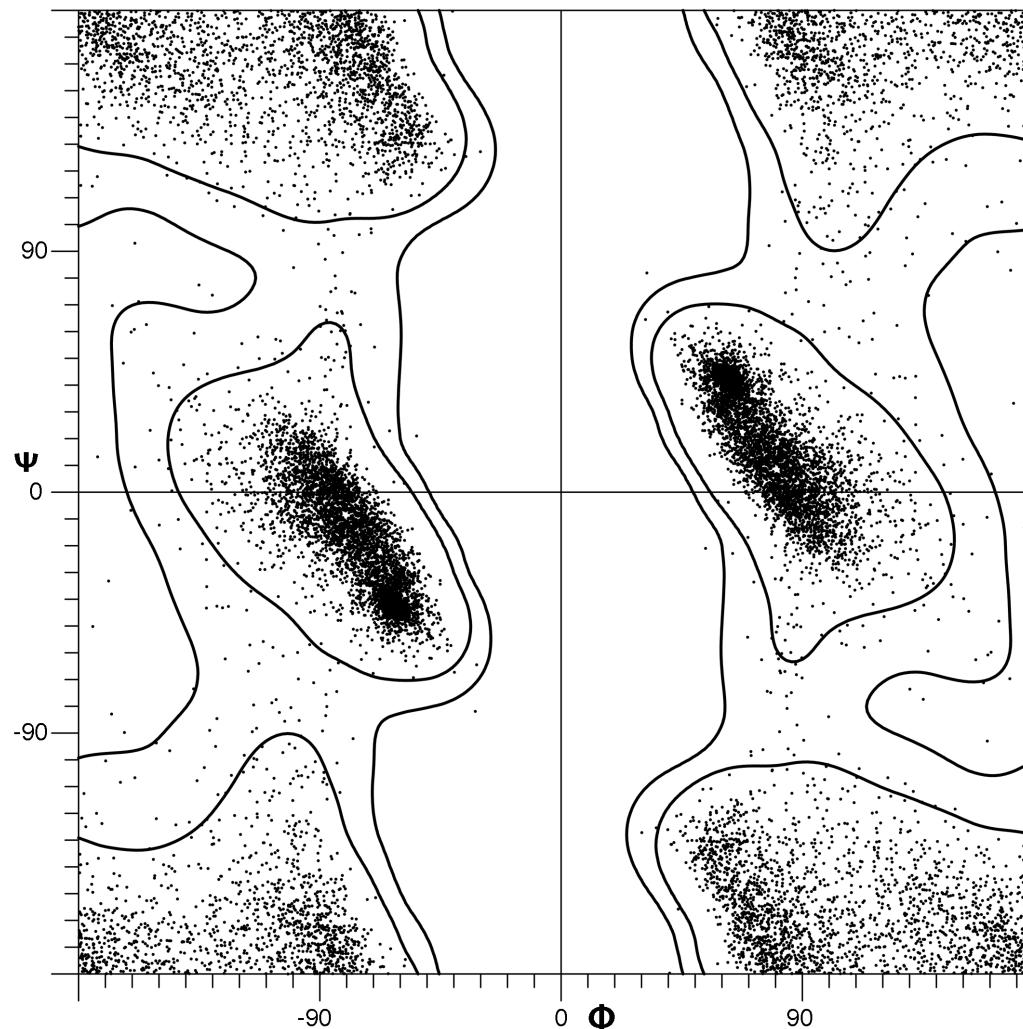
Ramachandran Plot



ϕ, ψ plot for over 80,000 well-ordered (i.e. $B \leq 30$) non-Gly, non-Pro, non pre-Pro residues in 500 proteins at 1.8 Å resolution or better (Lovell et al., 2003)

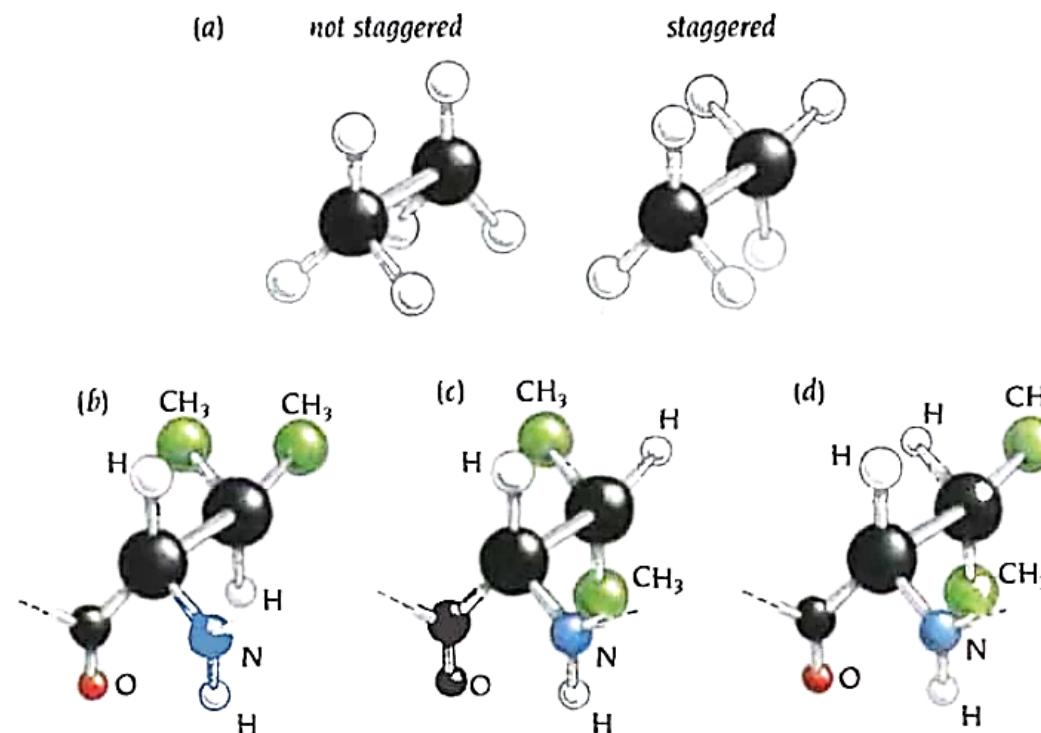


BIO331 Protein Structure and Function



Certain side-chain conformations are energetically favorable

- Residues having multiple side-chain conformations
 - Any side chain longer than that of Ala (C_β)
- Rotamer
 - Energetically favored conformation

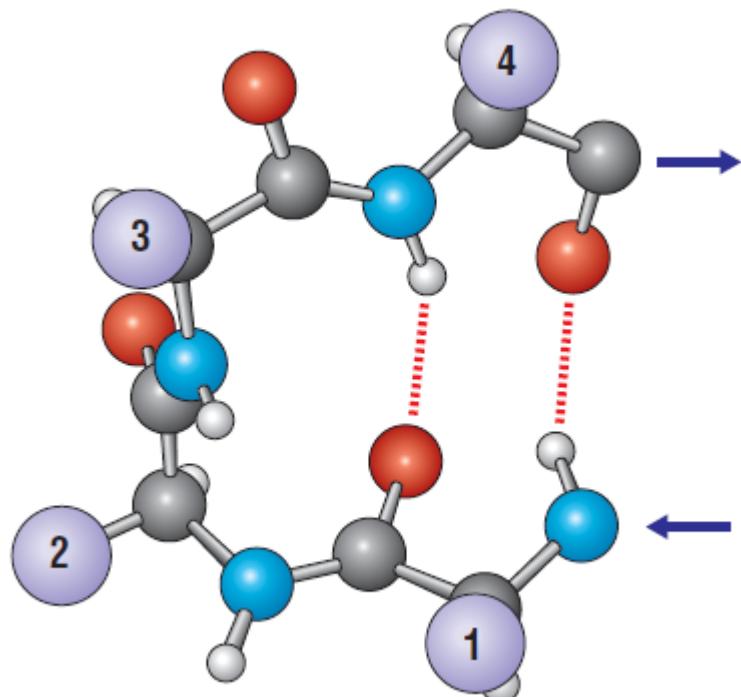


Secondary Structure Turn

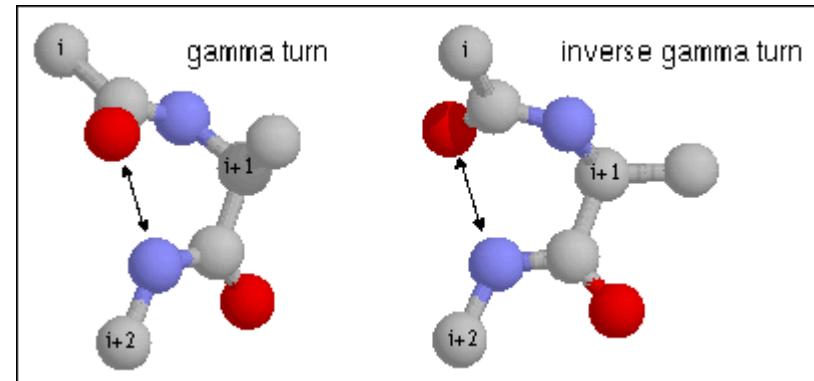
β -turn

Reverse turn or hairpin turn

Commonly having a proline at 2



γ -turn



Secondary Structure

α -helix

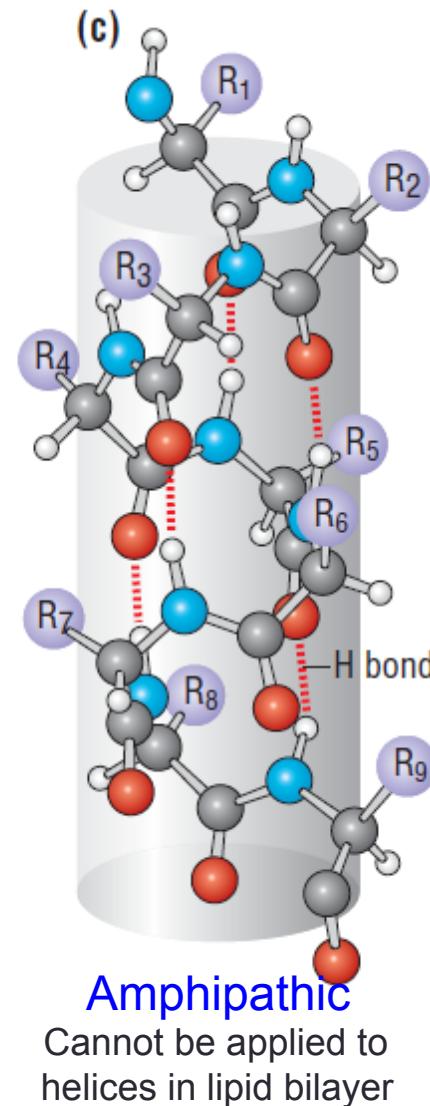
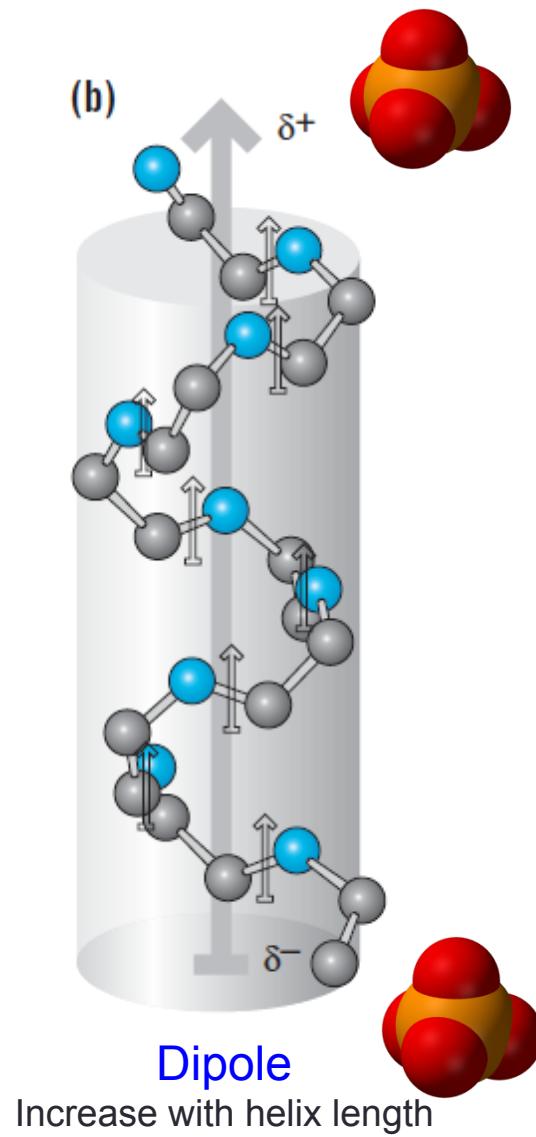
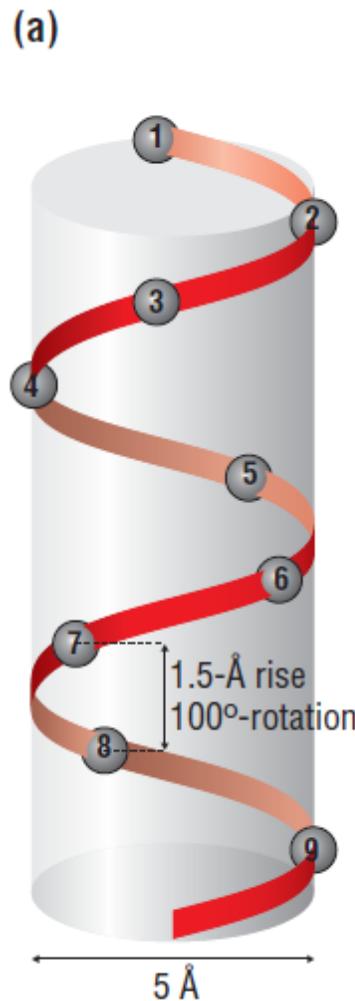


Table 2.1 Amino acid sequences of three α helices

1. - Leu - Ser - Phe - Ala - Ala - Ala - Met - Asn - Gly - Leu - Ala -
2. - Ile - Asn - Glu - Gly - Phe - Asp - Leu - Leu - Arg - Ser - Gly -
3. - Lys - Glu - Asp - Ala - Lys - Gly - Lys - Ser - Glu - Glu - Glu -

The first sequence is from the enzyme citrate synthase, residues 260–270, which form a buried helix; the second sequence is from the enzyme alcohol dehydrogenase, residues 355–365, which form a partially exposed helix; and the third sequence is from troponin-C, residues 87–97, which form a completely exposed helix. Charged residues are colored red, polar residues are blue, and hydrophobic residues are green.

Secondary Structure

Helical structures

Average Conformational Parameters of Helical Elements

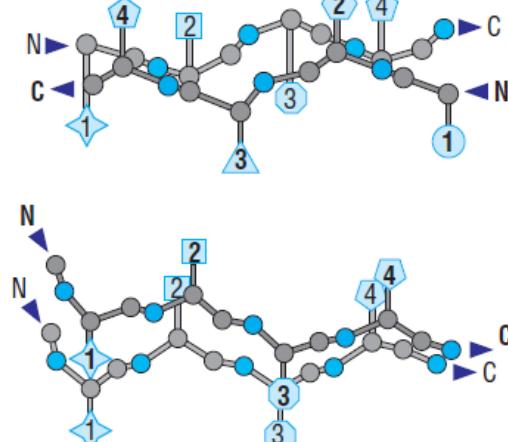
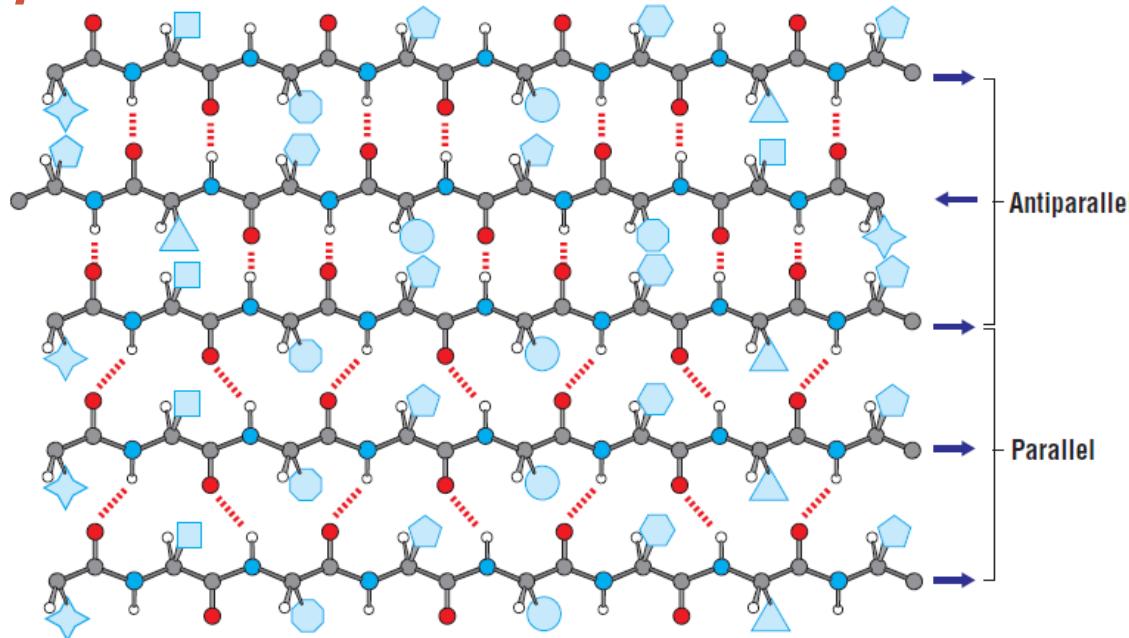
Conformation	Phi	Psi	Omega	Residues per turn	Translation per residue
Alpha helix	-57	-47	180	3.6	1.5
3-10 helix	-49	-26	180	3.0	2.0
Pi-helix	57	-70	180	4.4	1.15
Polyproline I	-83	+158	0	3.33	1.9
Polyproline II	-78	+149	180	3.0	3.12
Polyproline III	-80	+150	180	3.0	3.1

collagen triple helix



Secondary Structure

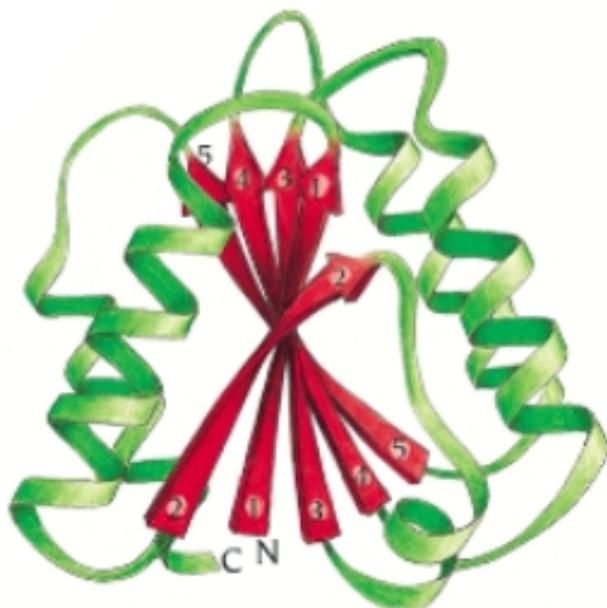
β -sheet



- Almost fully **extended**
- β -sheets on surfaces are **amphipathic** 两性
- **Antiparallel** vs. **parallel**
 - Stability: high vs. relatively low (weaker H-bonds)
 - Topology: continuous/discontinuous vs. discontinuous
 - Twist: more vs. less

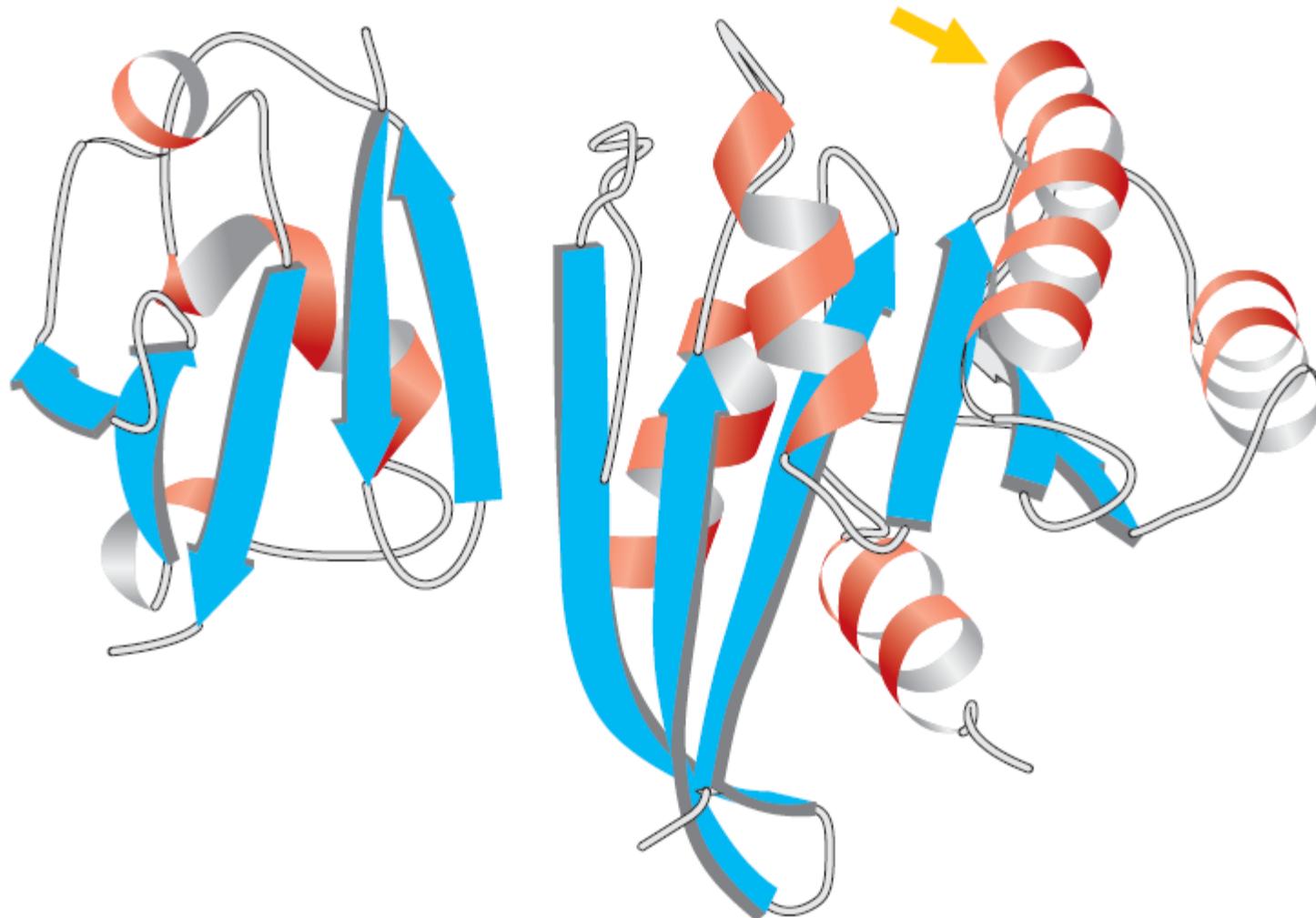
Secondary Structure

Twisted β-sheet

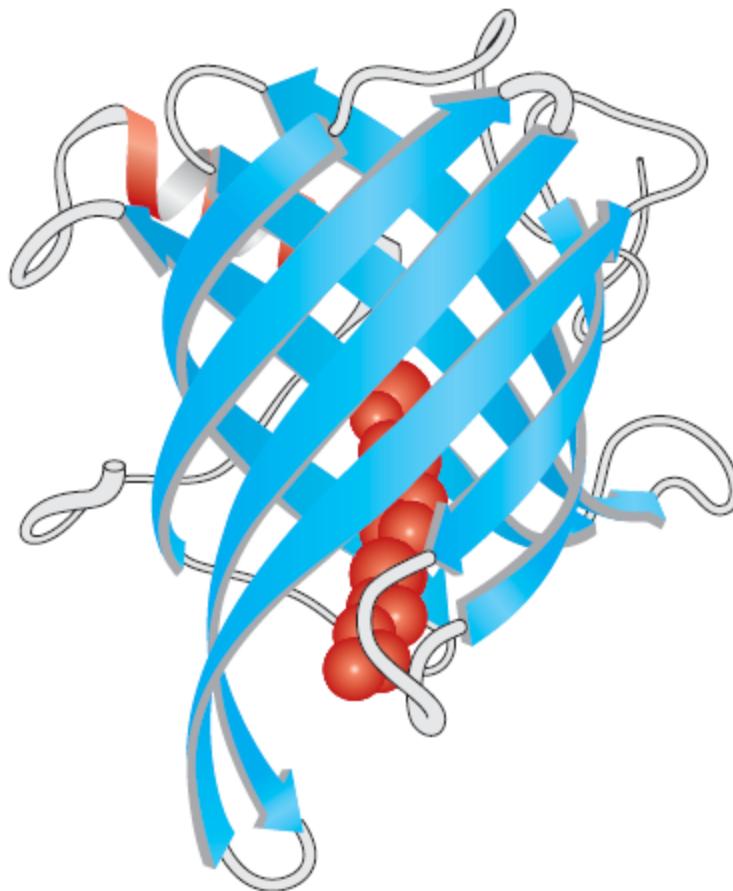


Lactate dehydrogenase

- Right-handed twist
 - steric effects
- Long strands are themselves twisted
- Interacting with other secondary structures or forming a barrel



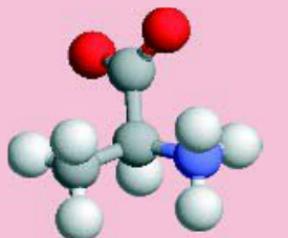
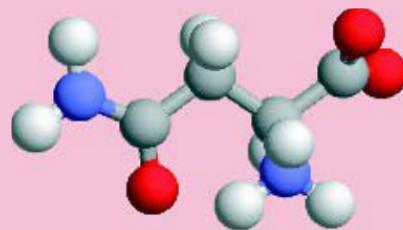
Two proteins that form a complex through hydrogen bonding between β -strands (the Rap–Raf complex, PDB **1GUA**)



β -barrel In the retinol-binding protein (PDB 1RLB)

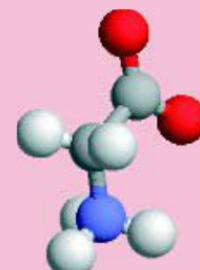
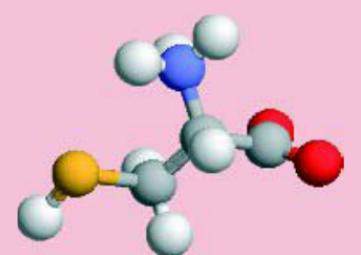
BIO331 Protein Structure and Function

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Alanine	Non-polar side chain.	
A	Small side chain volume.	
Ala	Van der Waals volume = 67 \AA^3	
M_r 71.09	Frequency in proteins = 7.7 % Surface area = 115 \AA^2 Unreactive side chain	
Arginine	Positively charged side chain at pH 7.0. pK	
R	for guanidino group in proteins ~ 12.0	
Arg	Van der Waals volume = 167 \AA^3	
M_r 156.19	Frequency in proteins = 5.1 % Surface area = 225 \AA^2 Participates in ionic interactions with negatively charged groups	
Asparagine	Polar, but uncharged, side chain	
N	Van der Waals volume = 148 \AA^3	
Asn	Frequency in proteins = 4.3 %	
M_r 114.11	Surface area = 160 \AA^2 Polar side chain will hydrogen bond Relatively small side chain volume leads to this residue being found relatively frequently in turns	
Aspartate	Negatively charged side chain	
D	pK for side chain of ~ 4.0	
Asp	Van der Waals volume = 67 \AA^3	
M_r 115.09	Frequency in proteins = 5.2 % Surface area = 150 \AA^2 Charged side chain exhibits electrostatic interactions with positively charged groups.	

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Cysteine	Side chain contains thiol (SH) group.
C	Van der Waals volume = 86 Å ³
Cys	Frequency in proteins = 2.0 %
M _r 103.15	Surface area = 135 Å ² Thiol side chain has pK in isolated amino acid of ~8.5 but in proteins varies 5–10 Thiol group is very reactive
Glutamine	Polar but uncharged side chain
Q	Van der Waals volume = 114 Å ³
Gln	Frequency in proteins = 4.1 %
M _r 128.12	Surface area = 180 Å ² Polar side chain can hydrogen bond
Glutamate	Negatively charged side chain.
E	Van der Waals volume = 109 Å ³
Glu	Frequency in proteins = 6.2 %
M _r 129.12	Surface area = 190 Å ² Side chain has pK of ~4.5.
Glycine	Uncharged, small side chain.
G	Often found in turn regions of proteins or regions of conformational flexibility
Gly	No chiral centre; due to two hydrogens attached to C _α centre
M _r 57.05	Van der Waals volume = 48 Å ³ Frequency in proteins = 7.4 % Surface area = 75 Å ²



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Histidine

H

His

M_r 137.14

Imidazole side chain

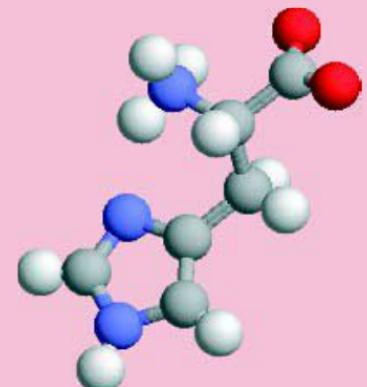
Van der Waals volume = 118 Å³

Frequency in proteins = 2.3 %

Surface area = 195 Å²

The side chain exhibits a pK ~ 6.0 in model

peptides but in proteins can vary from
4–10



Isoleucine

I

Ile

M_r 113.16

Hydrophobic side chain exhibiting non-polar
based interactions but generally unreactive

Van der Waals volume = 124 Å³

Frequency in proteins = 5.3 %

Surface area = 175 Å²



Leucine

L

Leu

M_r 113.16

Hydrophobic side chain

Van der Waals volume = 124 Å³

Frequency in proteins = 8.5 %

Surface area = 170 Å²



Lysine

K

Lys

M_r 128.17

Positively charged side chain

Van der Waals volume = 135 Å³

Frequency in proteins = 5.9 %

Surface area = 200 Å²

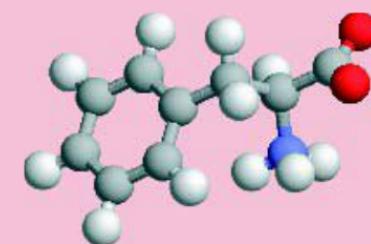
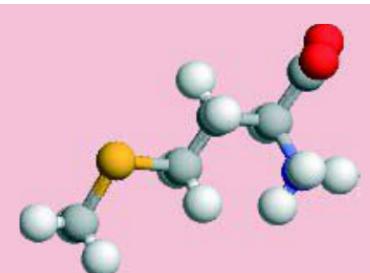
Side chain is basic with pK of ~10.5.

Shows ionic interactions



BIO331 Protein Structure and Function

Methionine M Met M_r 131.19	Sulfur containing hydrophobic side chain The sulfur is unreactive especially when compared with thiol group of cysteine Van der Waals volume = 124 \AA^3 Frequency in proteins = 2.4 % Surface area = 185 \AA^2
Phenylalanine F Phe M_r 147.18	Hydrophobic, aromatic side chain Phenyl ring is chemically unreactive in proteins. Exhibits weak optical absorbance around 280 nm Van der Waals volume = 135 \AA^3 Frequency in proteins = 4.0 % Surface area = 210 \AA^2
Proline P Pro M_r 97.12	Cyclic ring forming hydrophobic side chain The cyclic ring limits conformational flexibility around N-C _α bond In a polypeptide chain lacks amide hydrogen and cannot form backbone hydrogen bonds Van der Waals volume = 90 \AA^3 Frequency in proteins = 5.1 % Surface area = 145 \AA^2
Serine S Ser M_r 87.08	Polar but uncharged side chain. Contains hydroxyl group (-OH) that hydrogen bonds Oxygen atom can act as potent nucleophile in some enzymes Van der Waals volume = 73 \AA^3 Frequency in proteins = 6.9 % Surface area = 115 \AA^2



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Threonine T	Polar but uncharged side chain. Contains hydroxyl group (-OH)
Thr	Hydrogen bonding side chain
M_r 101.11	Van der Waals volume = 93 \AA^3 Frequency in proteins = 5.9 % Surface area = 140 \AA^2
Tryptophan W	Large, hydrophobic and aromatic side chain Almost all reactivity is based around the indole ring nitrogen Responsible for majority of near uv absorbance in proteins at 280 nm
Trp	Van der Waals volume = 163 \AA^3 Frequency in proteins = 1.4 % Surface area = 255 \AA^2
Tyrosine Y	Aromatic side chain Van der Waals volume = 141 \AA^3 Frequency in proteins = 3.2 % Surface area = 230 \AA^2 Phenolic hydroxyl group ionizes at pH values around pH 10 Aromatic ring more easily substituted than that of phenylalanine
Valine V	Hydrophobic side chain Van der Waals volume = 105 \AA^3 Frequency in proteins = 6.6 % Surface area = 155 \AA^2

