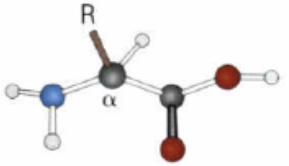
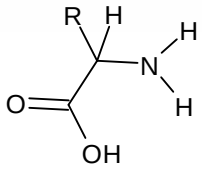
Proteins
&
Peptides

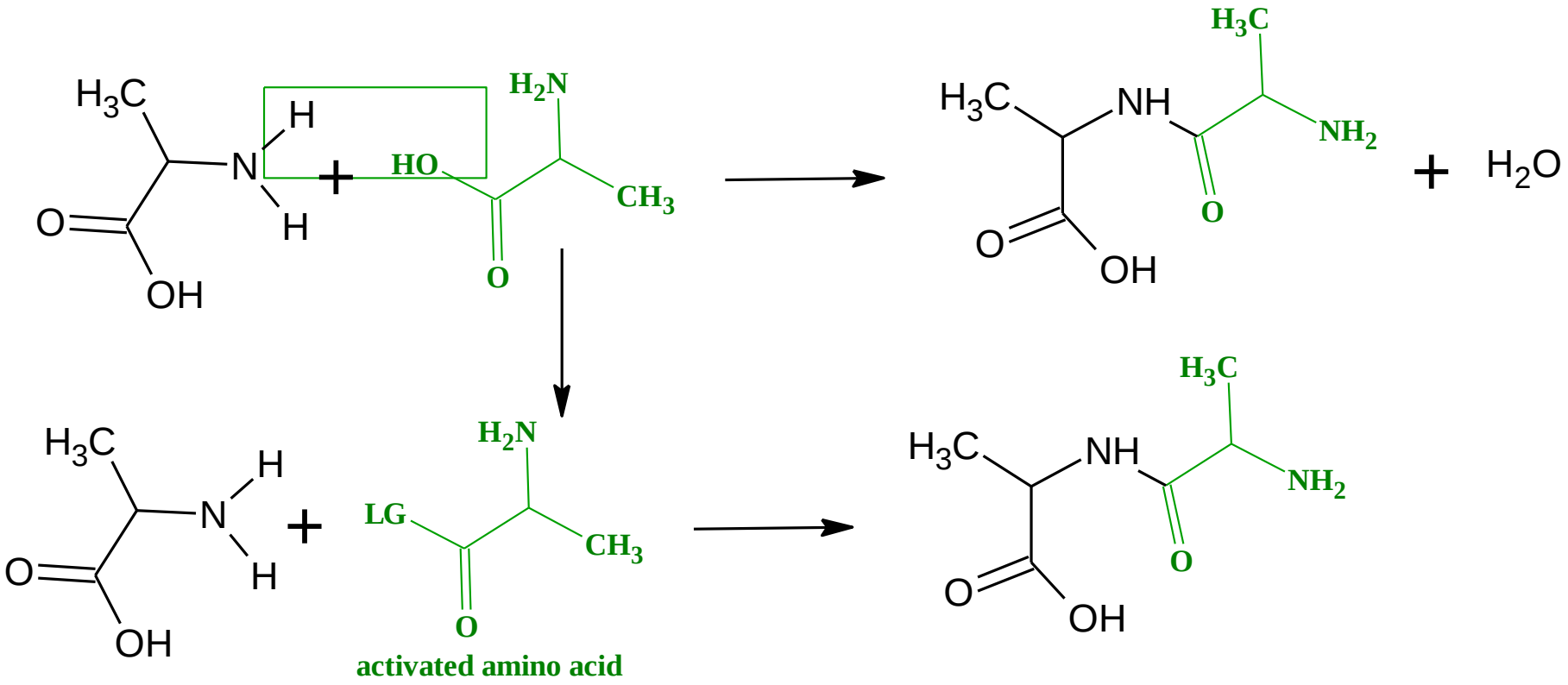
Peptide Backbone



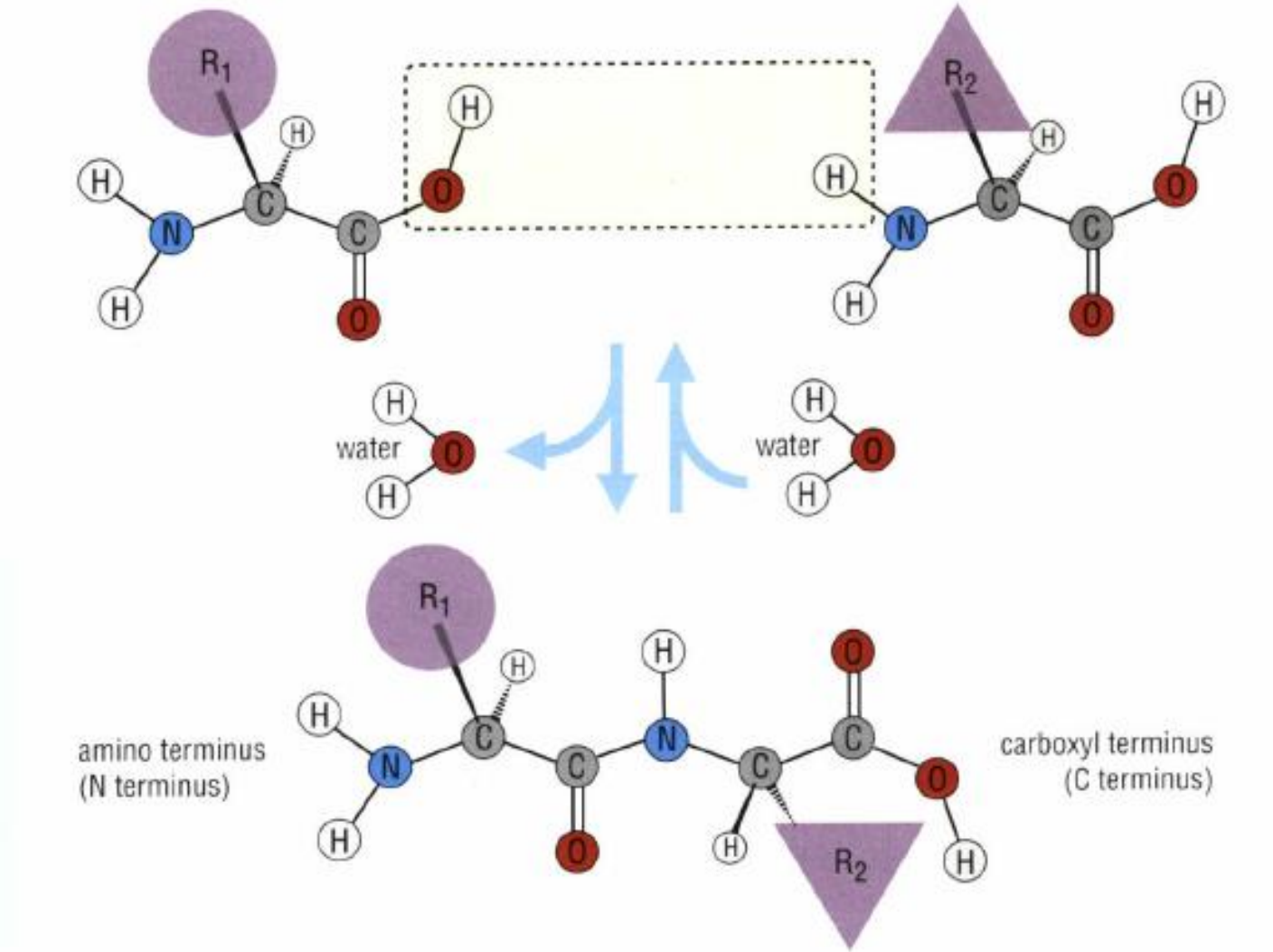


- Amino acid sequence
- Hydrophobic side chain: *Van der Waals interactions*
- Hydrophilic side chain: hydrogen bonding
- Amphoteric side chain
- Helix favoring residues: Ala & Leu

Amide Bond in Peptide Synthesis

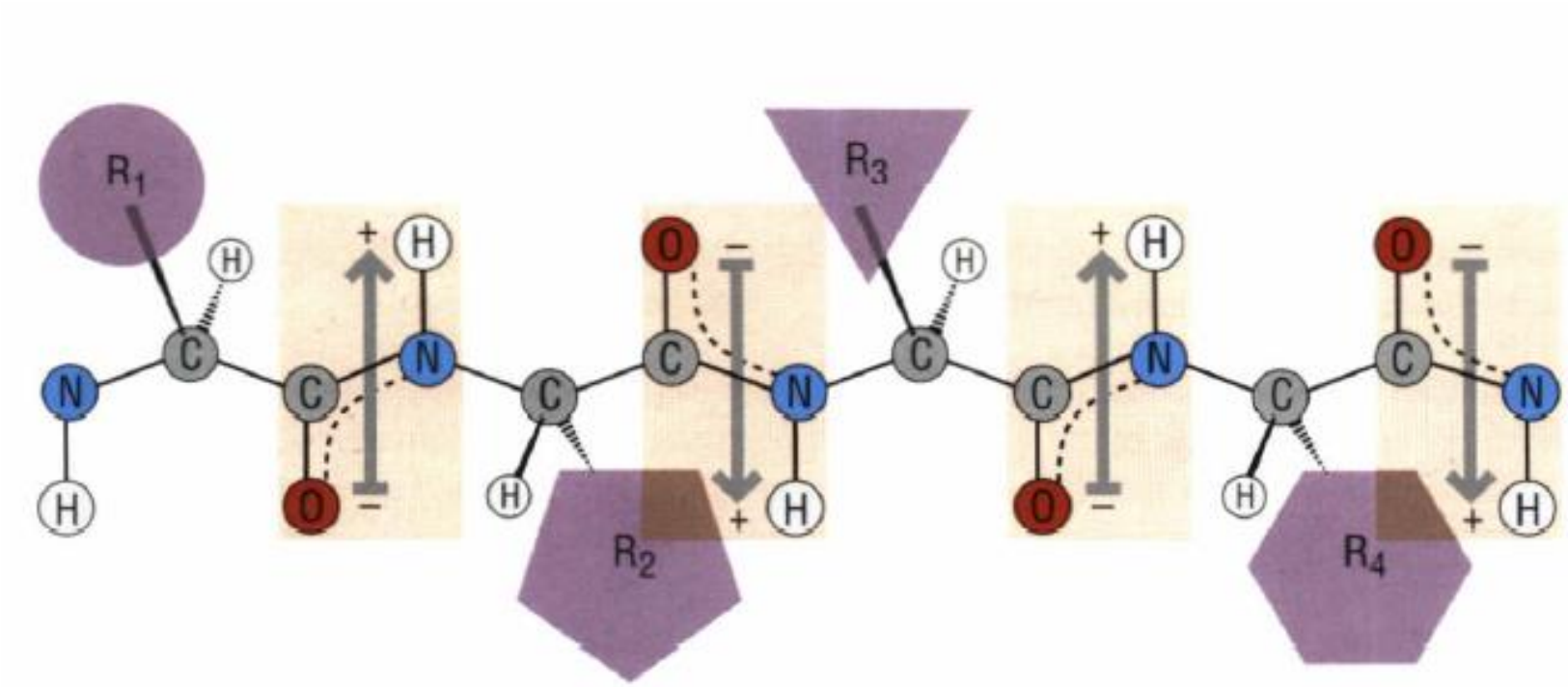


Peptide Bond



Schematic of an Extended Peptide Chain

- Consider amide bond tautomery in peptide sequence.



Conformations for Peptide: cis & trans

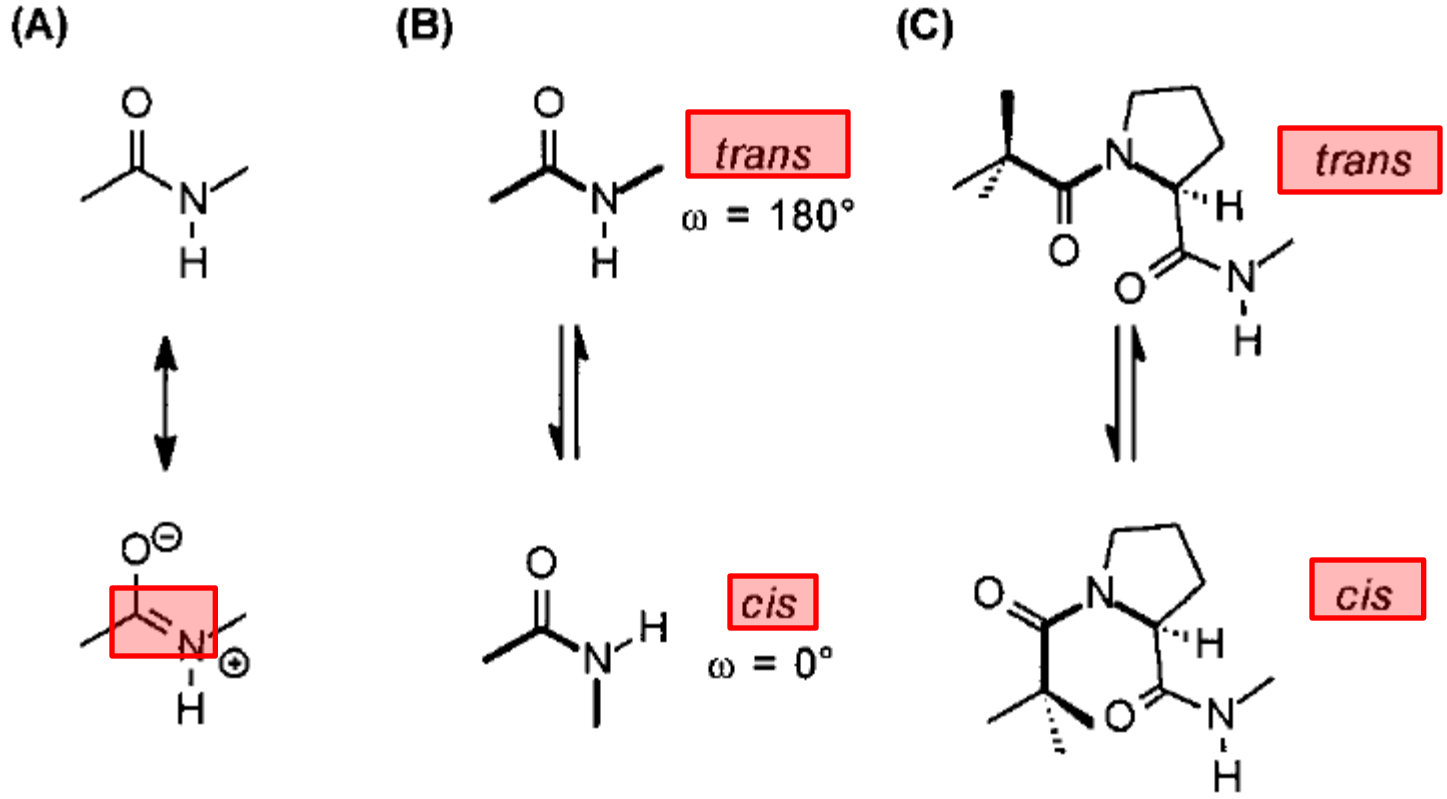


Fig. 2.2 (A) Resonance stabilization and (B) *cis/trans* isomerization of the peptide bond (C) *cis/trans* Isomers of a Xaa-Pro bond.

Chemistry and Biology. Norbert Sewald, Hans-Dieter Jakubke

Three Types of Bond Angles in Peptide Sequence

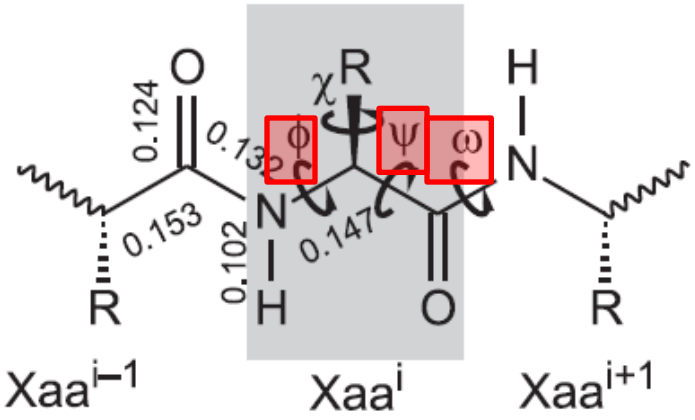
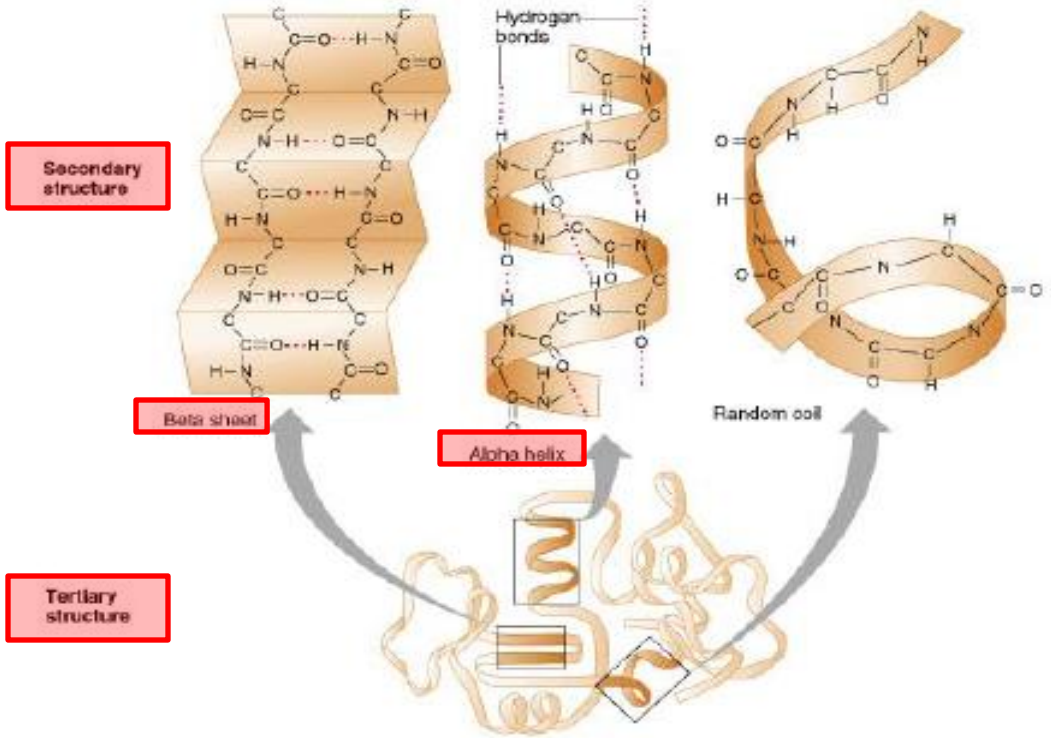
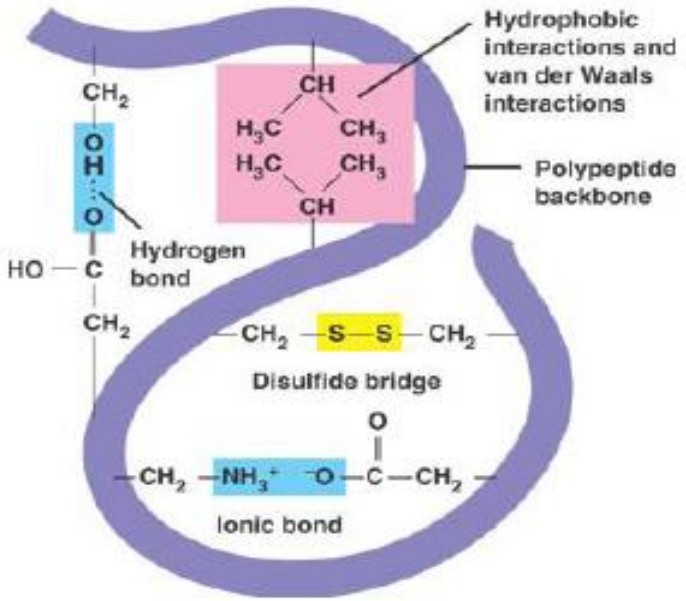


Fig. 2.1 Torsion angles φ, ψ, ω, and χ^1 and bond lengths of the amino acid Xaa^i in a peptide.

Structures Introduced for Proteins

Primary : sequence of amino acids
Secondary : backbone; Hydrogen bonds
Tertiary : side chain interactions
Quaternary : 2+ polypeptides

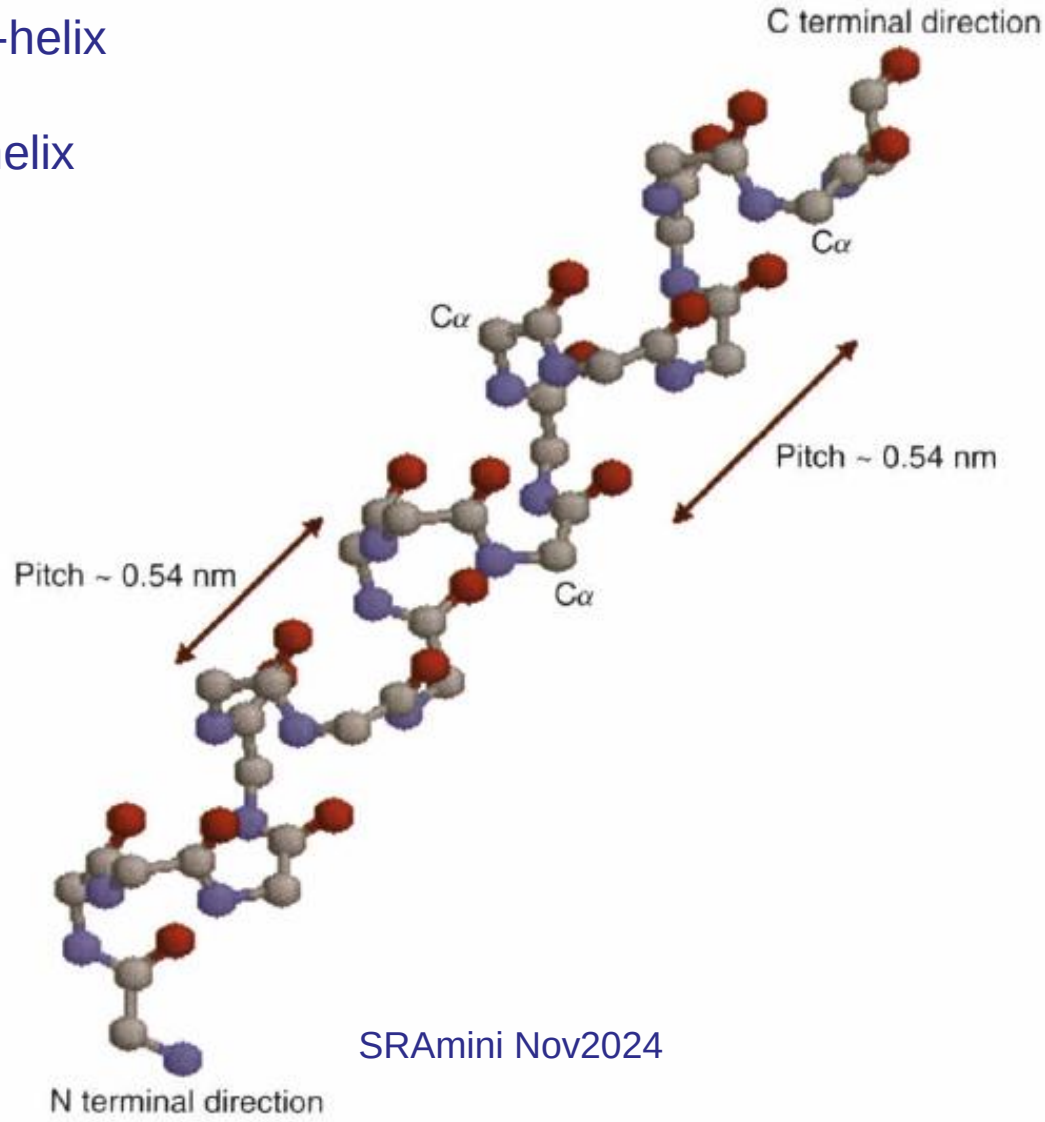




α-Helix as Secondary Structure of Protein

Right handed α-helix

Left handed α-helix



β-sheet as Secondary Structure of Protein

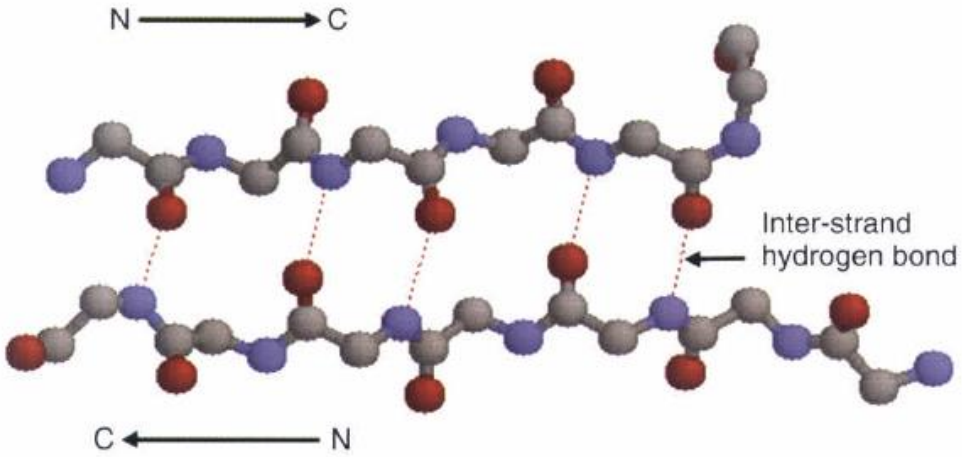


Figure 3.11 Two adjacent β strands are hydrogen bonded to form a small element of β sheet. The hydrogen bonds are inter-strand between neighbouring CO and NH groups. Only the heavy atoms are shown in this diagram for clarity

List of Essential Amino Acids

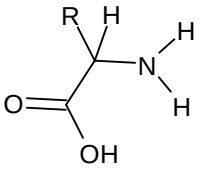


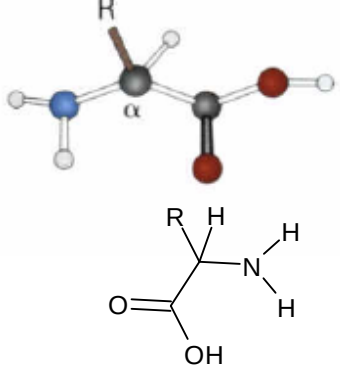
Table 2.1 The p*K* values for the α-carboxyl, α-amino groups and side chains found in the individual amino acids

Amino acid	pK_1	pK_2	pK_R	Amino acid	pK_1	pK_2	pK_R
Alanine	2.4	9.9	–	Leucine	2.3	9.7	–
Arginine	1.8	9.0	12.5	Lysine	2.2	9.1	10.5
Asparagine	2.1	8.7	–	Methionine	2.1	9.3	–
Aspartic Acid	2.0	9.9	3.9	Phenylalanine	2.2	9.3	–
Cysteine	1.9	10.7	8.4	Proline	2.0	10.6	–
Glutamic Acid	2.1	9.5	4.1	Serine	2.2	9.2	–
Glutamine	2.2	9.1	–	Threonine	2.1	9.1	–
Glycine	2.4	9.8	–	Tyrosine	2.2	9.2	10.5
Histidine	1.8	9.3	6.0	Tryptophan	2.5	9.4	–
Isoleucine	2.3	9.8	–	Valine	2.3	9.7	–

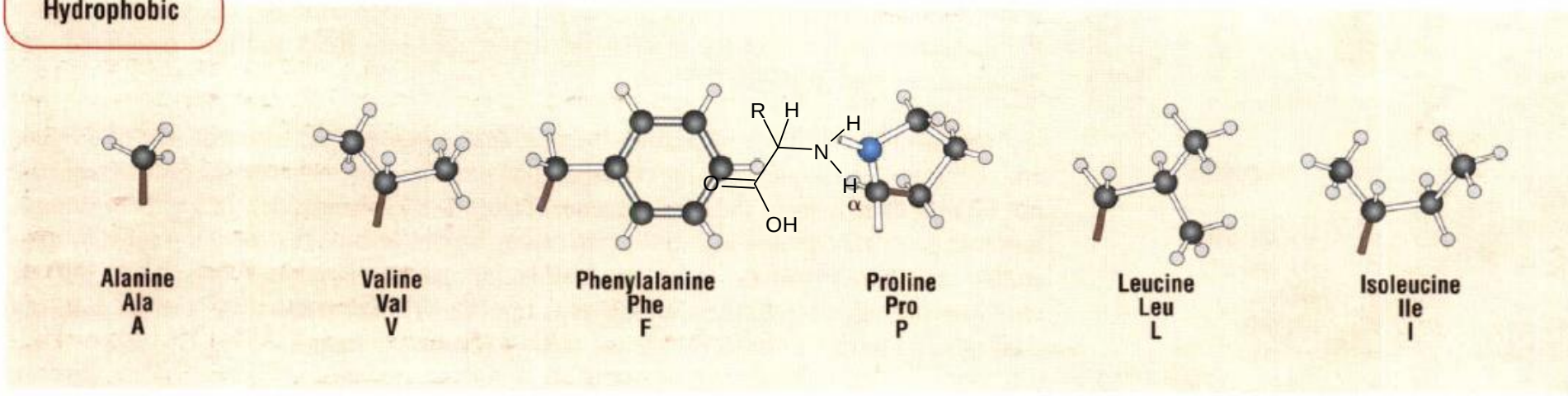
Adapted from Dawson, R.M.C, Elliot, W.H., & Jones, K.M. 1986 *Data for Biochemical Research*, 3rd edn. Clarendon Press Oxford.

From whitford

Hydrophobic α-Amino Acids



Hydrophobic



Alanine
Ala
A

Valine
Val
V

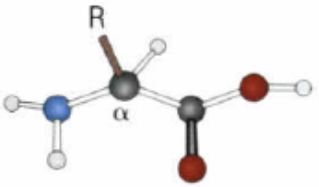
Phenylalanine
Phe
F

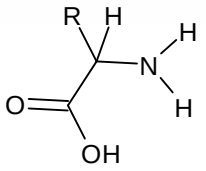
Proline
Pro
P

Leucine
Leu
L

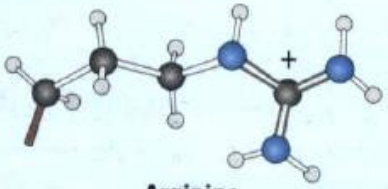
Isoleucine
Ile
I

Hydrophilic α-Amino Acids

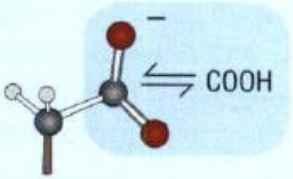




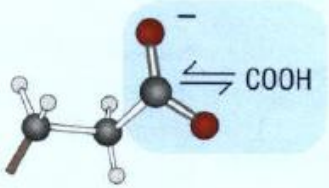
Hydrophilic



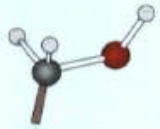
Arginine
Arg
R



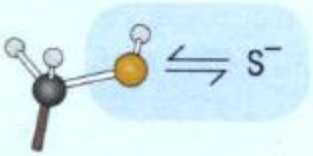
Aspartic acid
Asp
D



Glutamic acid
Glu
E

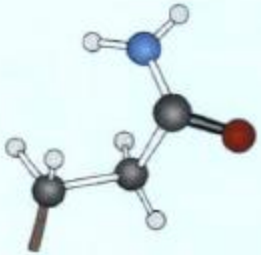


Serine
Ser
S

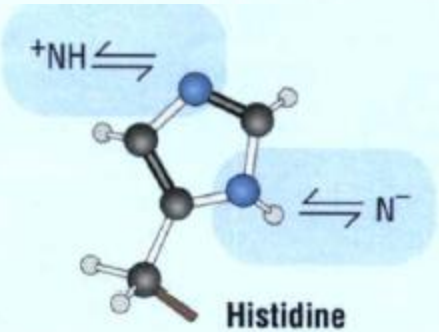


Cysteine
Cys
C

Asparagine
Asn
N

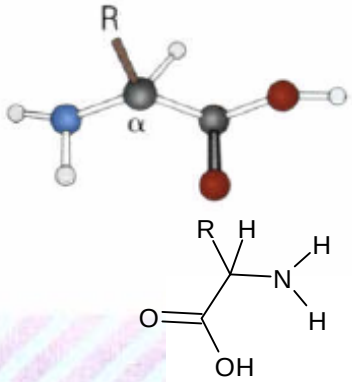


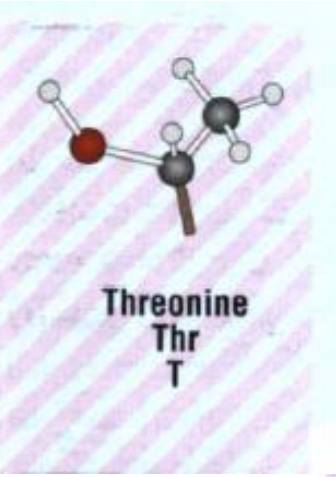
Glutamine
Gln
Q

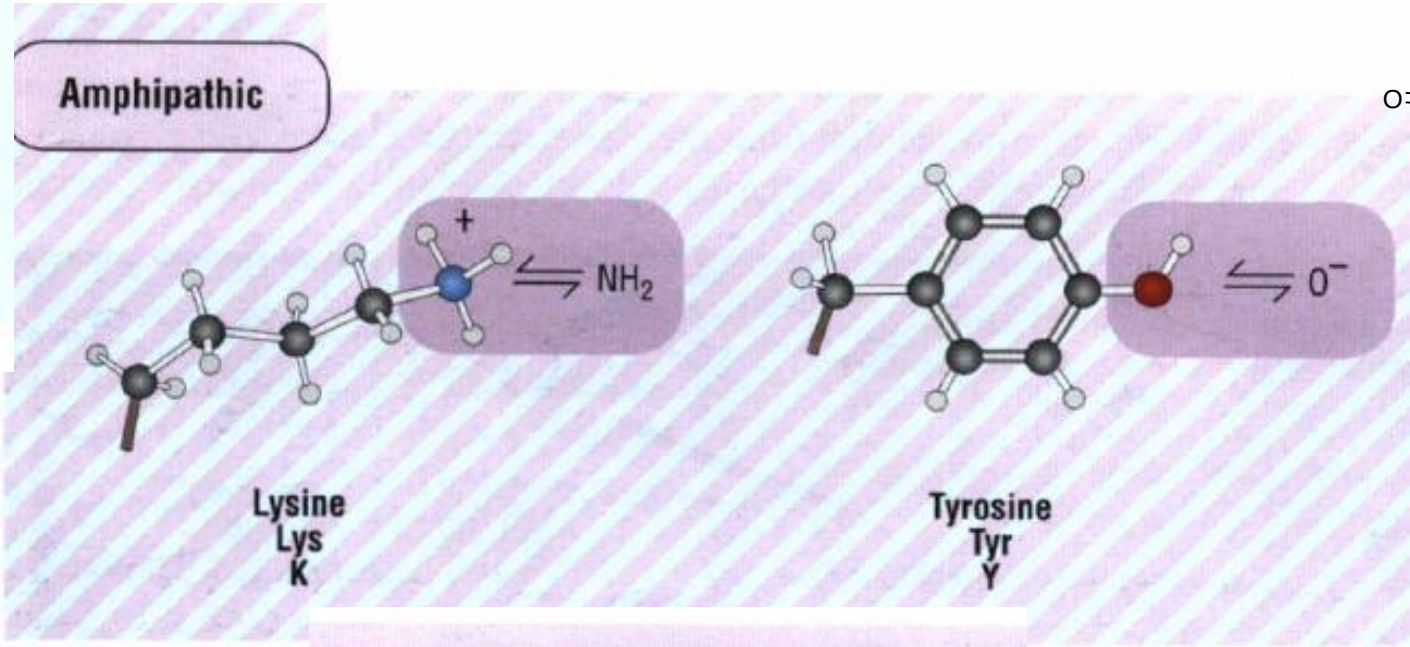


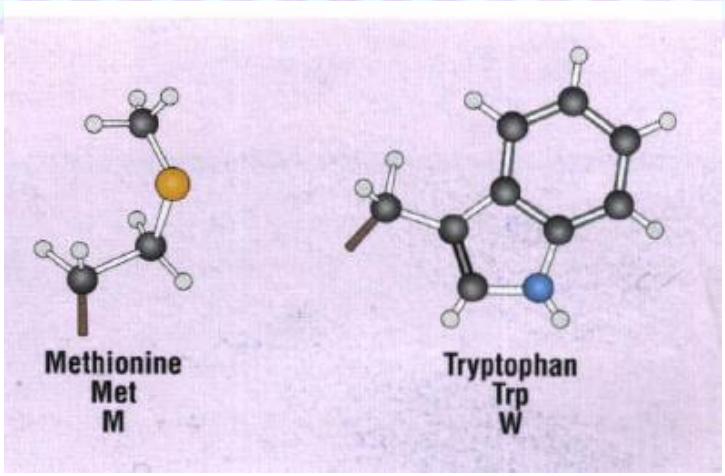
Histidine
His
H

Some Other α-Amino Acids

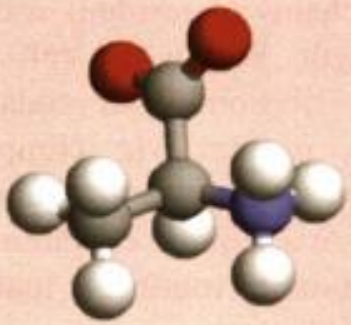
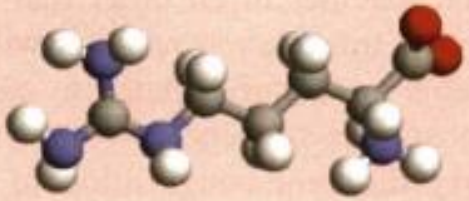






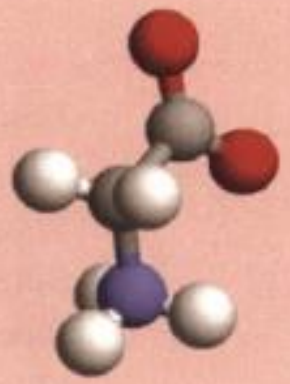


Physicochemical Properties of Essential α-Amino Acids

Amino acid	Property of individual amino acid residues	Ball and stick representation of each amino acid
Alanine A Ala M_r 71.09	Non-polar side chain. Small side chain volume. Van der Waals volume = 67 Å^{3*} Frequency in proteins = 7.7 % Surface area = 115 Å^2 Unreactive side chain	
Arginine R Arg M_r 156.19	Positively charged side chain at pH 7.0. pK for guanidino group in proteins ~12.0 Van der Waals volume = 167 Å^3 Frequency in proteins = 5.1 % Surface area = 225 Å^2 Participates in ionic interactions with negatively charged groups	

Physicochemical Properties of Essential α-Amino Acids- Contd.

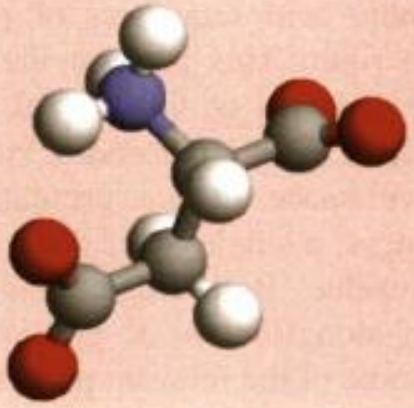
Glycine G Gly M_r 57.05	Uncharged, small side chain. Often found in turn regions of proteins or regions of conformational flexibility No chiral centre; due to two hydrogens attached to C_α centre Van der Waals volume = 48 Å^3 Frequency in proteins = 7.4 % Surface area = 75 Å^2



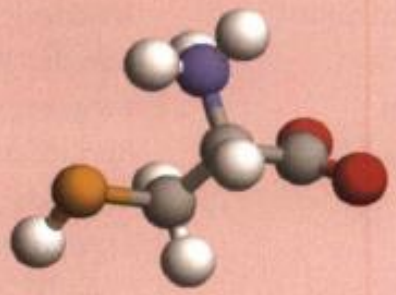
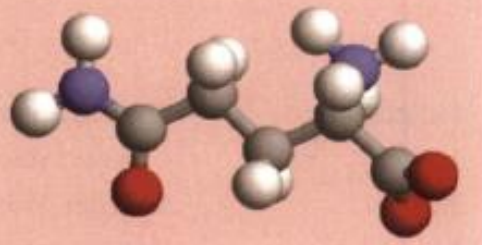
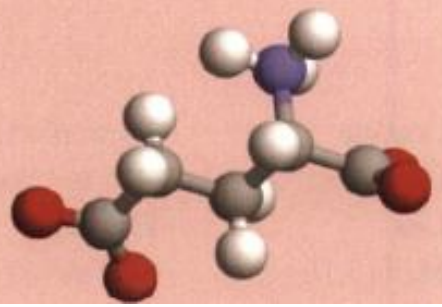
Physicochemical Properties of Essential α-Amino Acids- Contd.

Asparagine	Polar, but uncharged, side chain
N	Van der Waals volume = 148 Å^3
Asn	Frequency in proteins = 4.3 %
M_r 114.11	Surface area = 160 Å^2
	Polar side chain will hydrogen bond
	Relatively small side chain volume leads to this residue being found relatively frequently in turns

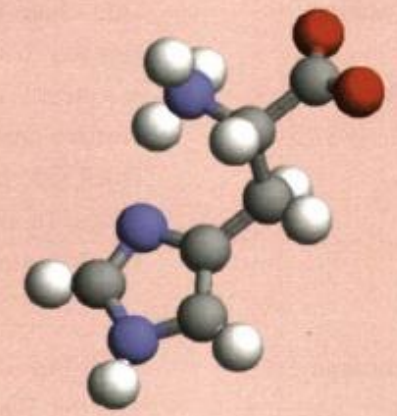
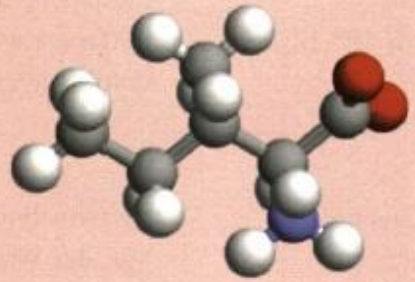
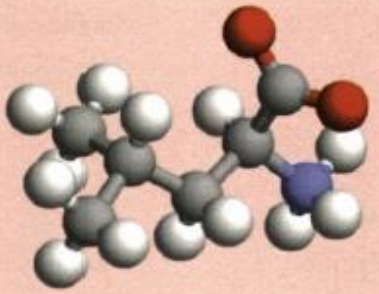
Aspartate	Negatively charged side chain
D	pK for side chain of ~4.0
Asp	Van der Waals volume = 67 Å^3
M_r 115.09	Frequency in proteins = 5.2 %
	Surface area = 150 Å^2
	Charged side chain exhibits electrostatic interactions with positively charged groups.



Physicochemical Properties of Essential α-Amino Acids- Contd.

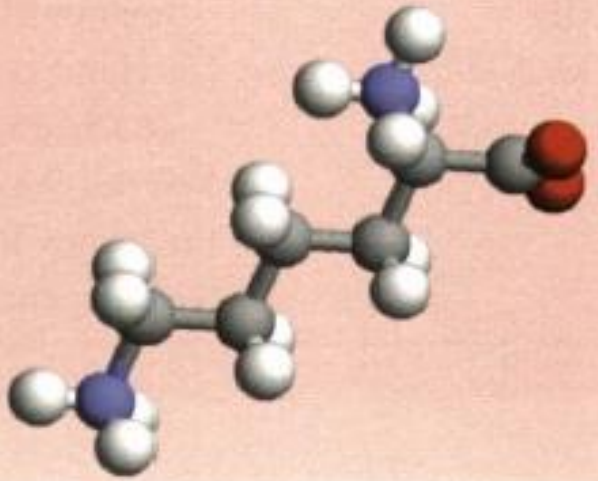
Amino acid	Property of individual amino acid residues	Ball and stick representation of each amino acid
Cysteine C Cys M_r 103.15	Side chain contains thiol (SH) group. Van der Waals volume = 86 Å^3 Frequency in proteins = 2.0 % Surface area = 135 Å^2 Thiol side chain has pK in isolated amino acid of ~8.5 but in proteins varies 5–10 Thiol group is very reactive	
Glutamine Q Gln M_r 128.12	Polar but uncharged side chain Van der Waals volume = 114 Å^3 Frequency in proteins = 4.1 % Surface area = 180 Å^2 Polar side chain can hydrogen bond	
Glutamate E Glu M_r 129.12	Negatively charged side chain. Van der Waals volume = 109 Å^3 Frequency in proteins = 6.2 % Surface area = 190 Å^2 Side chain has pK of ~4.5.	

Physicochemical Properties of Essential α-Amino Acids- Contd.

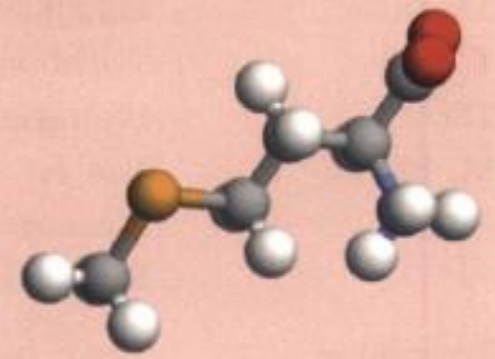
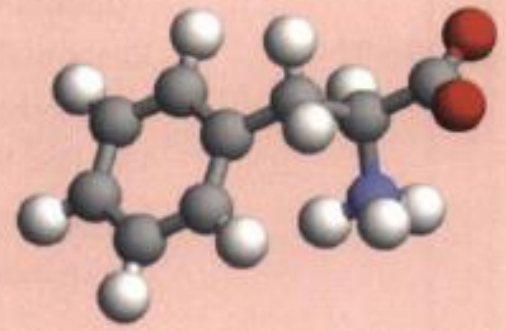
Amino acid	Property of individual amino acid residues	Ball and stick representation of each amino acid
Histidine H His M_r 137.14	Imidazole side chain Van der Waals volume = 118 Å^3 Frequency in proteins = 2.3 % Surface area = 195 Å^2 The side chain exhibits a pK ~ 6.0 in model peptides but in proteins 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 Å^3 Frequency in proteins = 5.3 % Surface area = 175 Å^2	
Leucine L Leu M_r 113.16	Hydrophobic side chain Van der Waals volume = 124 Å^3 Frequency in proteins = 8.5 % Surface area = 170 Å^2	

Physicochemical Properties of Essential α-Amino Acids- Contd.

Lysine	Positively charged side chain
K	Van der Waals volume = 135 Å^3
Lys	Frequency in proteins = 5.9 %
M_r 128.17	Surface area = 200 Å^2
	Side chain is basic with pK of ~10.5.
	Shows ionic interactions

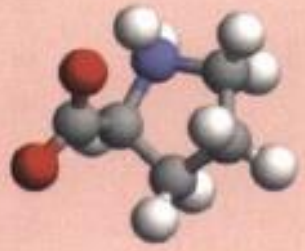


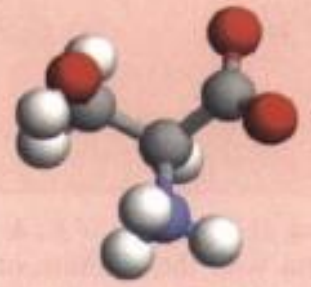
Physicochemical Properties of Essential α-Amino Acids- Contd.

Amino acid	Property of individual amino acid residues	Ball and stick representation of each amino acid
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 Å^3 Frequency in proteins = 2.4 % Surface area = 185 Å^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 Å^3 Frequency in proteins = 4.0 % Surface area = 210 Å^2	

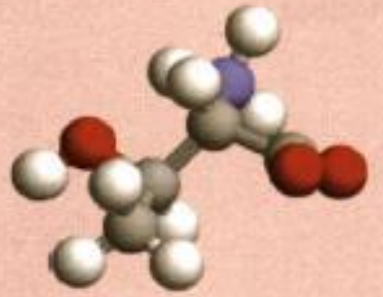
Physicochemical Properties of Essential α-Amino Acids- Contd.

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 Å^3 Frequency in proteins = 5.1 % Surface area = 145 Å^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 Å^3 Frequency in proteins = 6.9 % Surface area = 115 Å^2



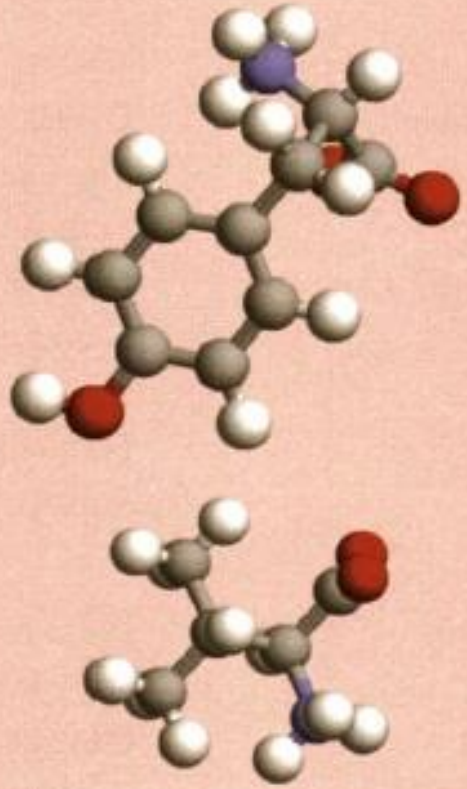


Physicochemical Properties of Essential α-Amino Acids- Contd.

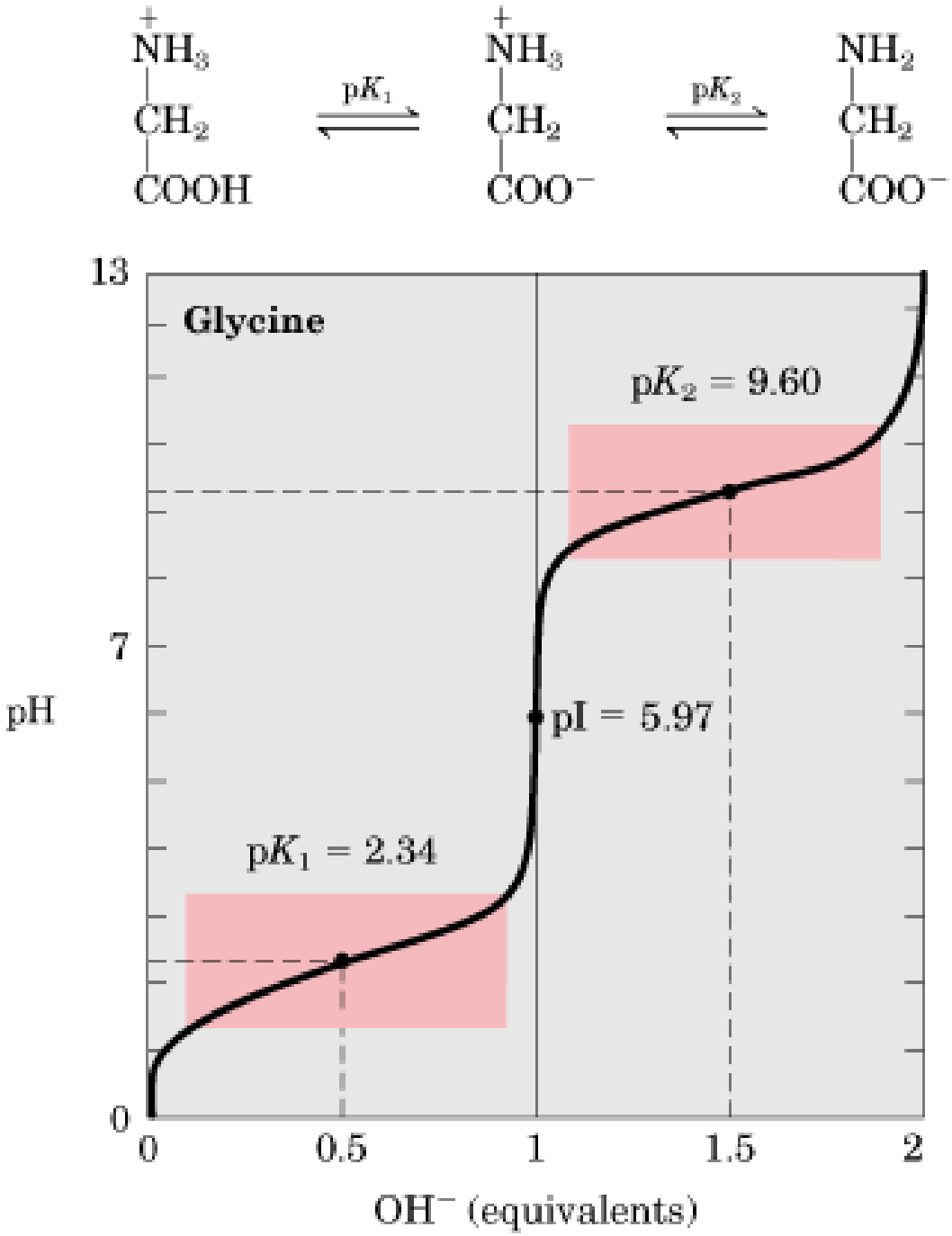
Amino acid	Property of individual amino acid residues	Ball and stick representation of each amino acid
Threonine T Thr M_r 101.11	Polar but uncharged side chain. Contains hydroxyl group (–OH) Hydrogen bonding side chain Van der Waals volume = 93 Å^3 Frequency in proteins = 5.9 % Surface area = 140 Å^2	
Tryptophan W Trp M_r 186.21	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 Van der Waals volume = 163 Å^3 Frequency in proteins = 1.4 % Surface area = 255 Å^2	

Physicochemical Properties of Essential α-Amino Acids- Contd.

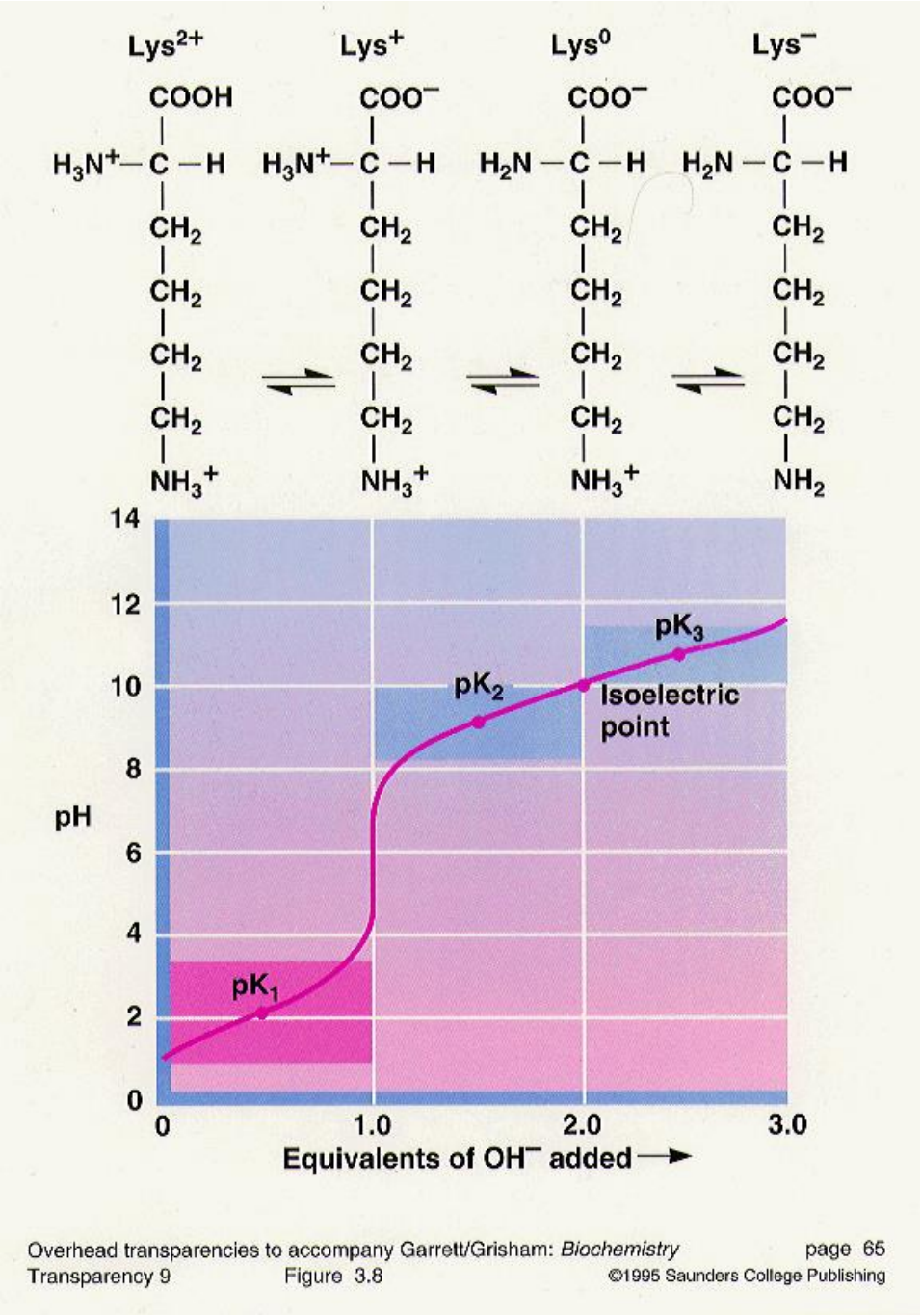
Tyrosine	Aromatic side chain
Y	Van der Waals volume = 141 Å^3
Tyr	Frequency in proteins = 3.2 %
M_r 163.18	Surface area = 230 Å^2
	Phenolic hydroxyl group ionizes at pH values around pH 10
	Aromatic ring more easily substituted than that of phenylalanine
Valine	Hydrophobic side chain
V	Van der Waals volume = 105 Å^3
Val	Frequency in proteins = 6.6 %
M_r 99.14	Surface area = 155 Å^2

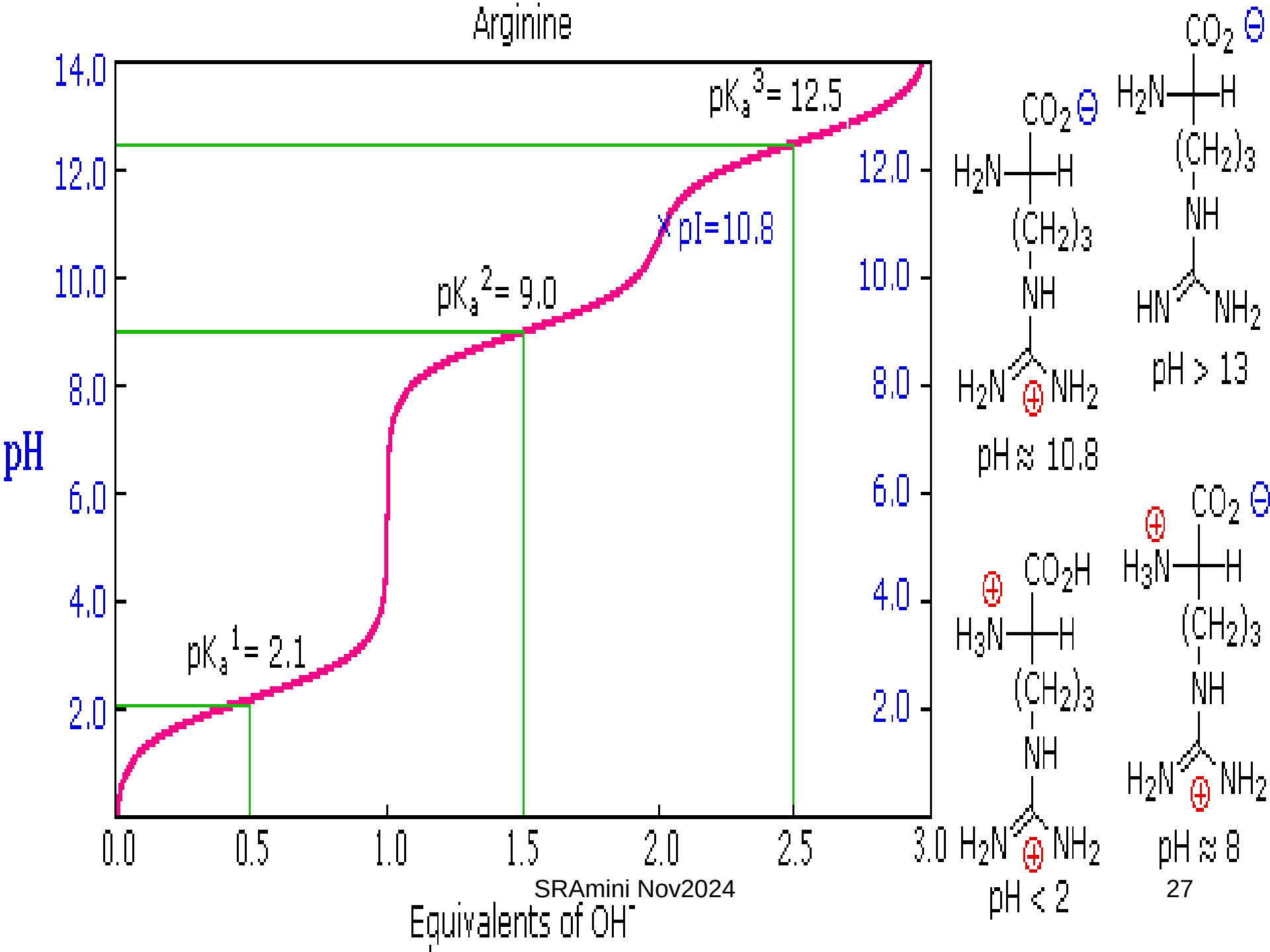


Quantitative Study via Titration of Gly as an α-Amino Acids with NaOH as Titrant



Quantitative Study via Titration of Lys as an α-Amino Acids with NaOH as Titrant




Arginine
pH
Equivalents of OH⁻
pK$_a^1$= 2.1
pK$_a^2$= 9.0
pK$_a^3$= 12.5
pI=10.8
pH > 13
pH ≈ 10.8
pH ≈ 8
pH < 2

Protein Analysis

- Purification:

✓ Electrophoresis: regarding pK_a & pI (isoelectric pH)

✓ chromatography

- Structure Elucidation:

✓ X- ray

✓ Circular Dichroism (CD)

✓ NMR

Protein Types

- Simple proteins

- Conjugated proteins:

✓ nucleoproteins
✓ glycoproteins
✓ phosphoproteins
✓ lipoproteins
✓ metalloproteins
✓ chromoproteins