Amino Acids, Peptides, and Proteins (Chapter 3)

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Protein functions :

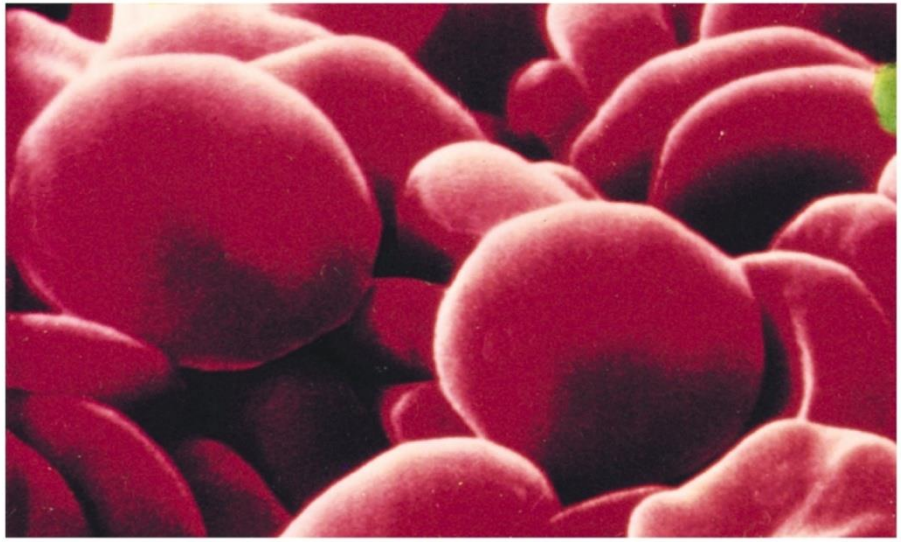
From 20 a.a cells make all proteins.

Enzymes, hormones, receptors,

Feathers, antibodies, muscle fibers,

mushroom poisons, transporting proteins

(hemoglobin), rhinoceros horns.



(b)

(c)

First a.a. asparagine 1806, Last threonine 1938.

Names derived from source of isolation:

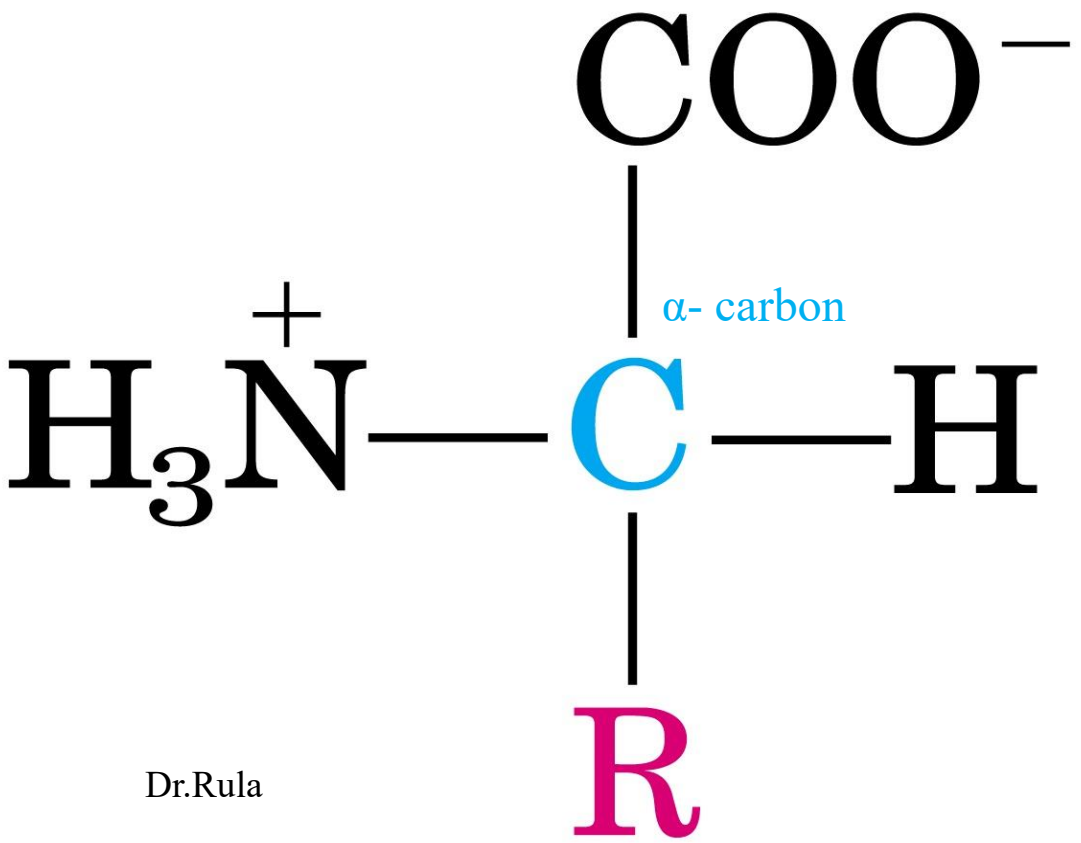
Asparagine = Asparagus

Tyrosine = cheese ‘tyros’ in greek

Glycine = ‘glycos’ in greek = sweet taste.

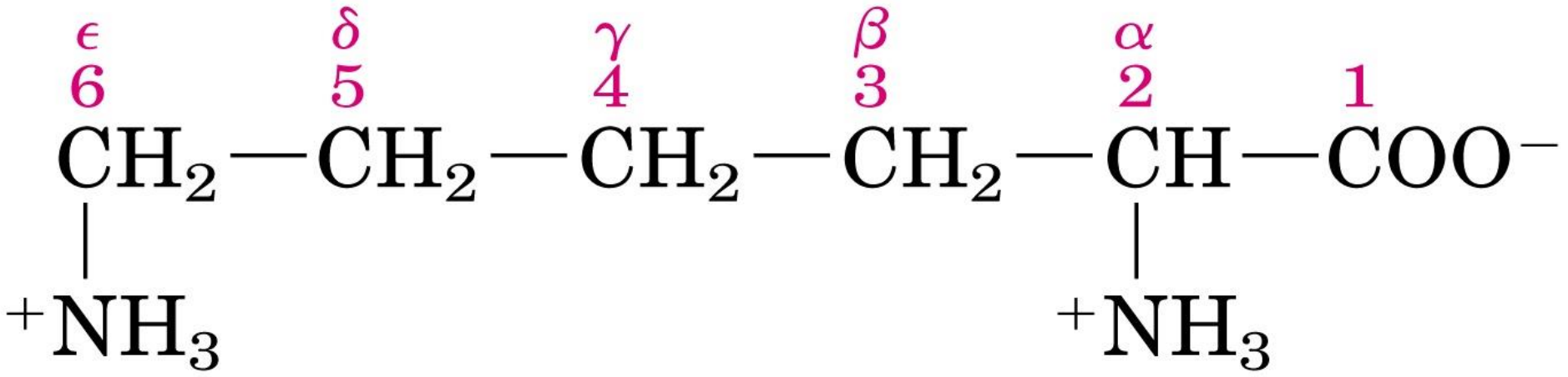
General structure of a.a (except proline):

Differ in R group affect structure, size, electric charge, solubility.



Two conventions used to identify the carbons in amino acids:

[----------R group----------]



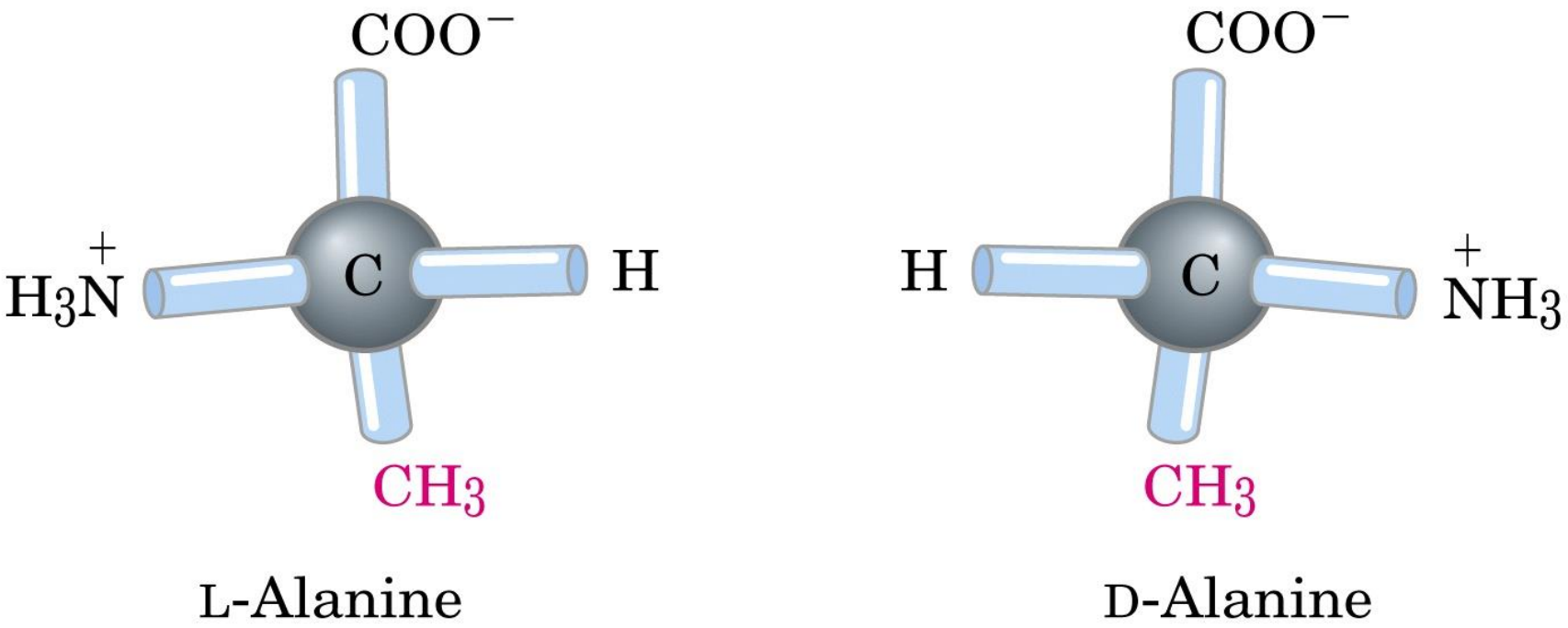
Lysine

Chiral center: α C bound to 4 different groups (except Gly)

Due to the tetrahedral arrangement around the α-carbon.

a.a. has 2 possible stereisomers = enantiomers. Nonsuperimposable=mirror images.

The absolute configuration of a.a and simple sugars D, L



all amino acids found in proteins

(a)

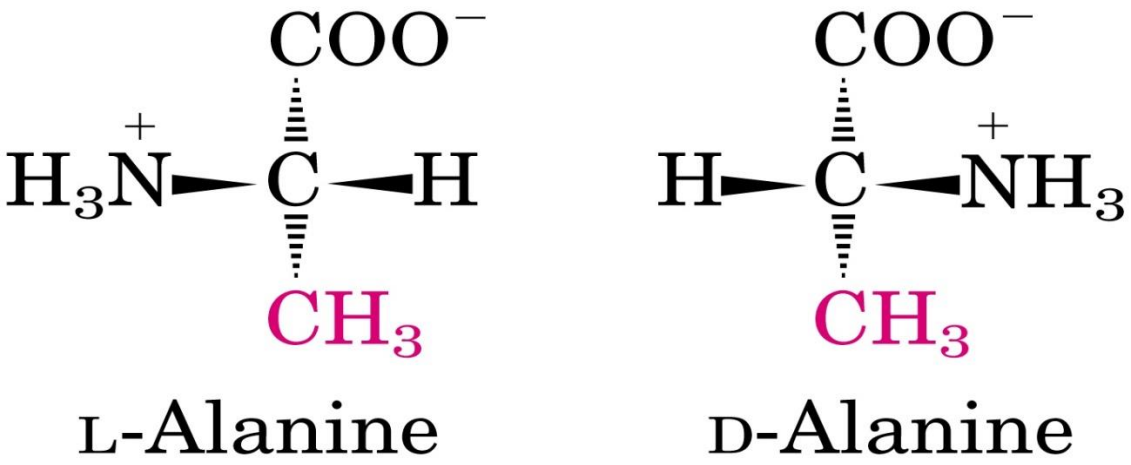
Stereoisomerism:

L-a.a. =

α amino group on the left

D- a.a. =

α amino group on the right



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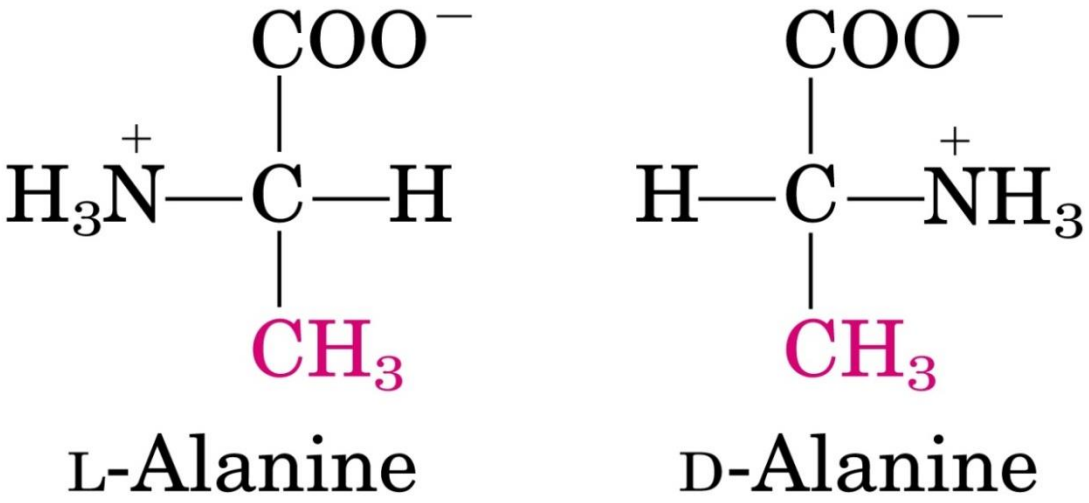
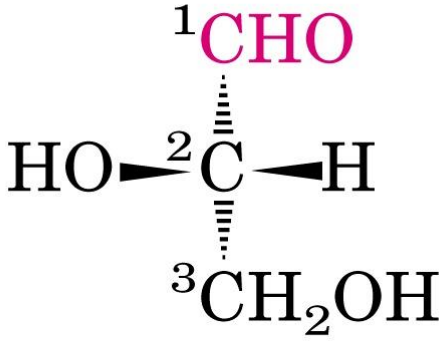


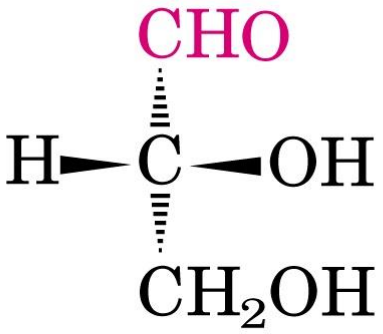
(c)

This configuration based on the reference molecule 3C sugar glyceraldehyde configuration.

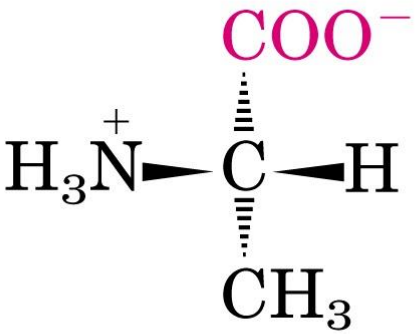
Carbons lined up vertically
with chiral atom in center
Terminal aldehyde/
carboxyl as number 1
The R group below the
chiral carbon.



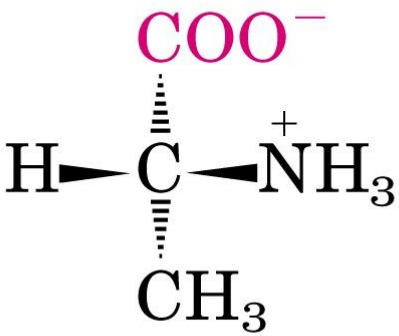
L-Glyceraldehyde



D-Glyceraldehyde



L-Alanine



D-Alanine

- All a.a. in proteins are exclusively L stereoisomers.

D- stereoisomers only in small peptides (peptide antibiotics, peptides of bacterial cell wall.

-Cells synthesize the L- isomer of a.a because the active sites of enzymes are asymmetric → the rxns they catalyze are sterospecific.

a.a classified into 5 types on the basis of:

polarity and charge (at pH = 7) of their R groups.

table 5–1

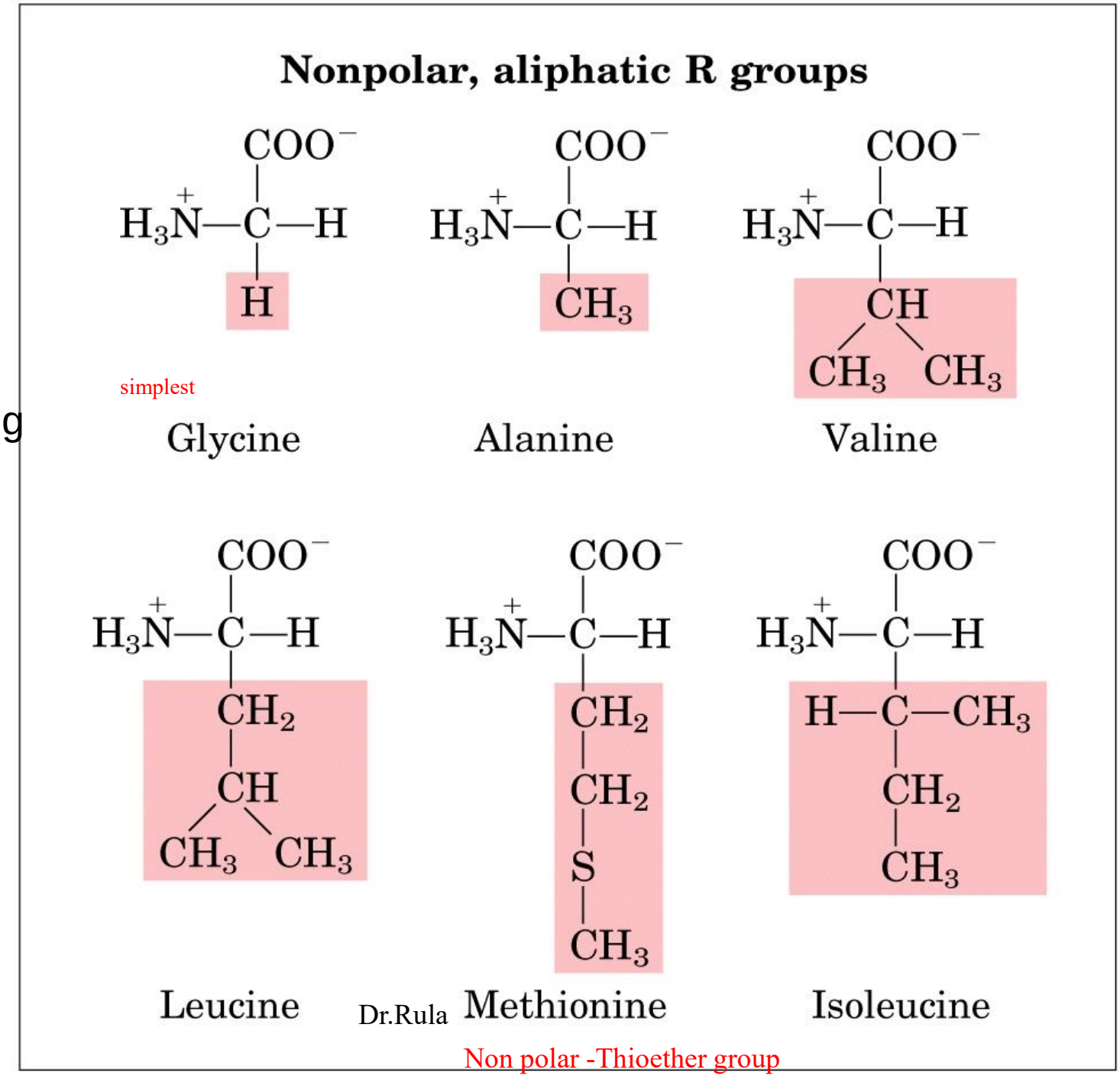
Properties and Conventions Associated with the Standard Amino Acids

Amino acid	Abbreviated names / symbol		M_r	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI	Hydropathy index*	Occurrence in proteins (%)
Nonpolar, aliphatic R groups									
Glycine	Gly	G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala	A	89	2.34	9.69		6.01	1.8	7.8
Valine	Val	V	117	2.32	9.62		5.97	4.2	6.6
Leucine	Leu	L	131	2.36	9.60		5.98	3.8	9.1
Isoleucine	Ile	I	131	2.36	9.68		6.02	4.5	5.3
Methionine	Met	M	149	2.28	9.21		5.74	1.9	2.3
Aromatic R groups									
Phenylalanine	Phe	F	165	1.83	9.13		5.48	2.8	3.9
Tyrosine	Tyr	Y	181	2.20	9.11	10.07	5.66	−1.3	3.2
Tryptophan	Trp	W	204	2.38	9.39		5.89	−0.9	1.4
Polar, uncharged R groups									
Serine	Ser	S	105	2.21	9.15		5.68	−0.8	6.8
Proline	Pro	P	115	1.99	10.96		6.48	1.6	5.2
Threonine	Thr	T	119	2.11	9.62		5.87	−0.7	5.9
Cysteine	Cys	C	121	1.96	10.28	8.18	5.07	2.5	1.9
Asparagine	Asn	N	132	2.02	8.80		5.41	−3.5	4.3
Glutamine	Gln	Q	146	2.17	9.13		5.65	−3.5	4.2
Positively charged R groups									
Lysine	Lys	K	146	2.18	8.95	10.53	9.74	−3.9	5.9
Histidine	His	H	155	1.82	9.17	6.00	7.59	−3.2	2.3
Arginine	Arg	R	174	2.17	9.04	12.48	10.76	−4.5	5.1
Negatively charged R groups									
Aspartate	Asp	D	133	1.88	9.60	3.65	2.77	−3.5	5.3
Glutamate	Glu	E	147	2.19	9.67	4.25	3.22	−3.5	6.3

*A scale combining hydrophobicity and hydrophilicity of R groups; it can be used to measure the tendency of an amino acid to seek an aqueous environment (− values) or a hydrophobic environment (+ values). See Chapter 12. From Kyte, J. & Doolittle, R.F. (1982) *J. Mol. Biol.* **157,** 105 – 132.

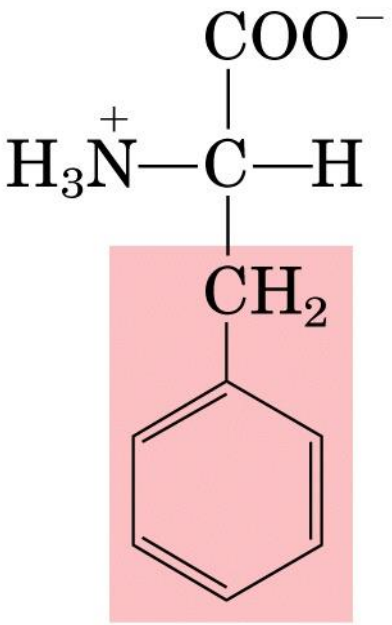
†Average occurrence in over 1150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed) Plenum Press, NY, pp. 599–623.

The hydrophobic (water-insoluble) side chains of these a.a cluster together stabilizing protein structure .



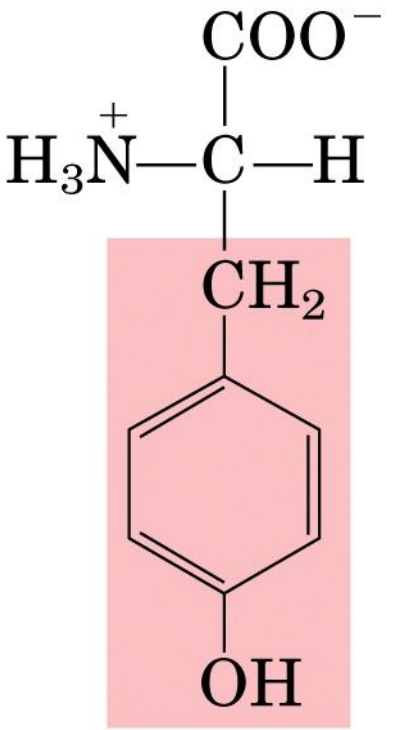
Absorb UV at 280nm

Aromatic R groups



Phenylalanine

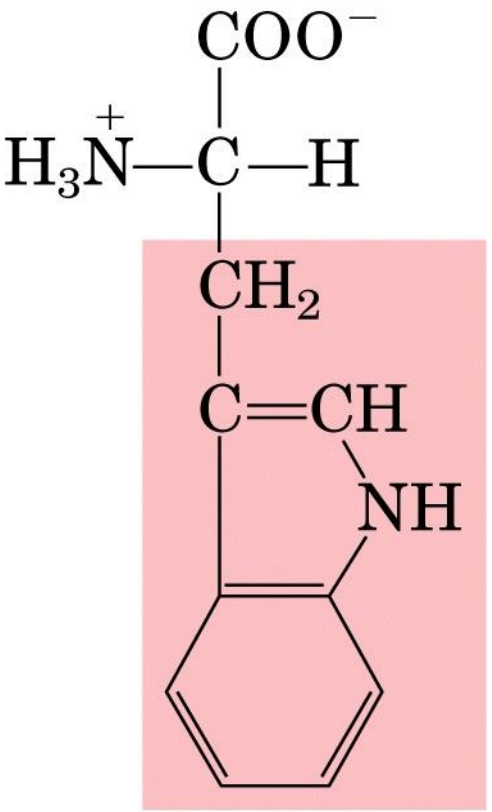
Nonpolar



Hydroxyl form H-bond.
Important in E active site

Tyrosine

Polar hydroxyl



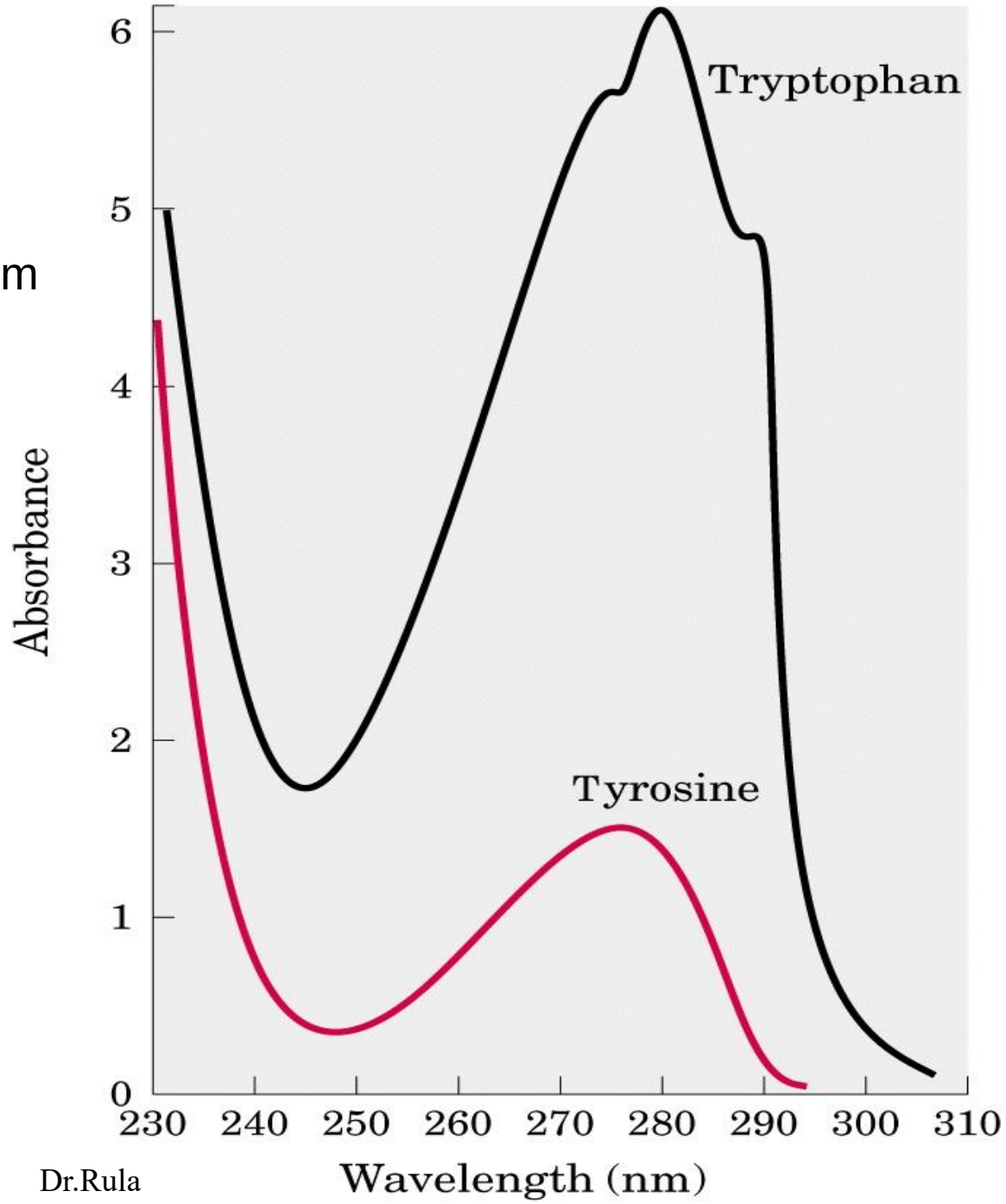
Tryptophan

polar nitrogen of indole ring

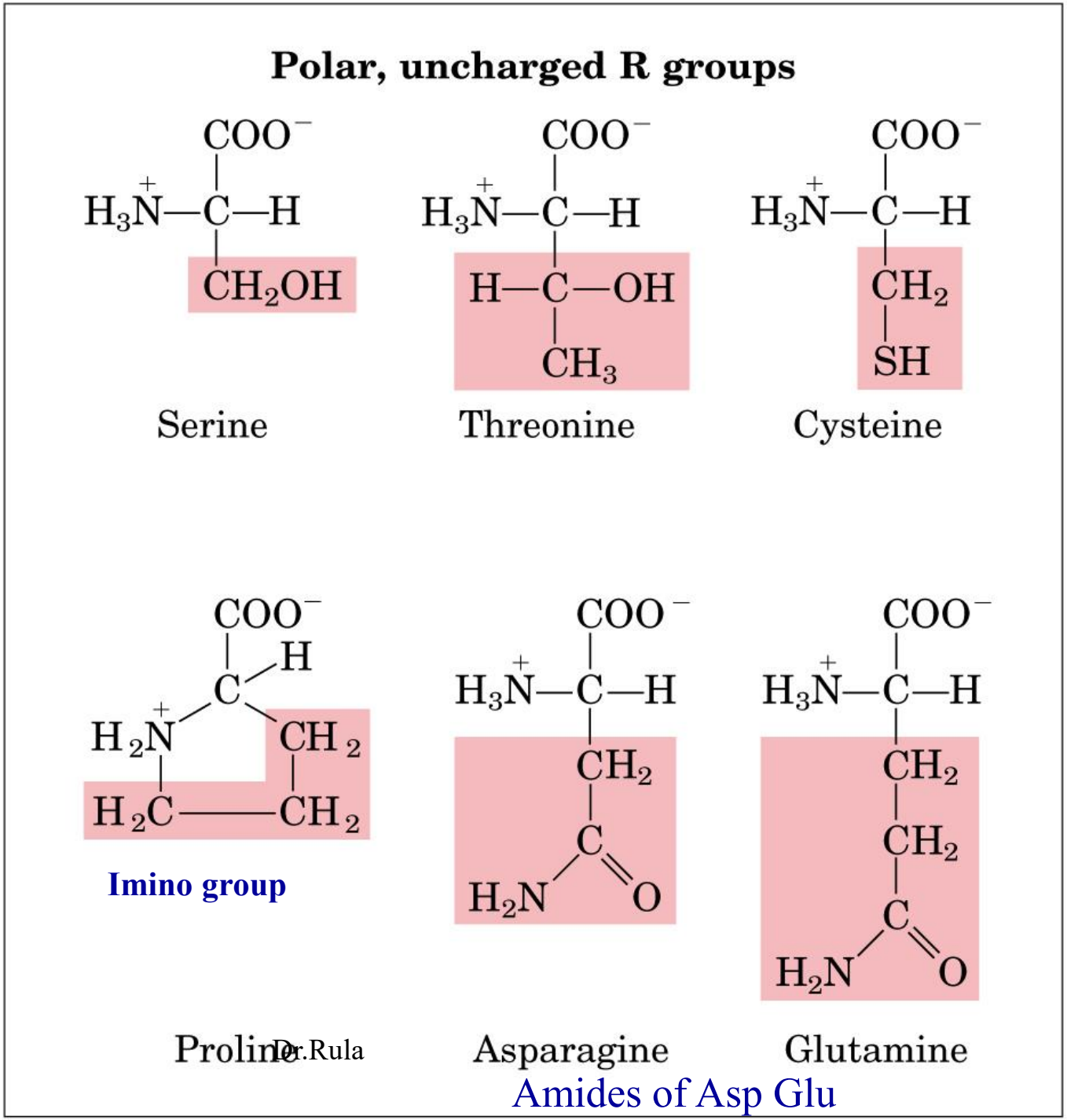
Absorption of UV light by aromatic a.a :

Maximum absorbance at 280nm

Tryptophan 4 times>> tyrosine

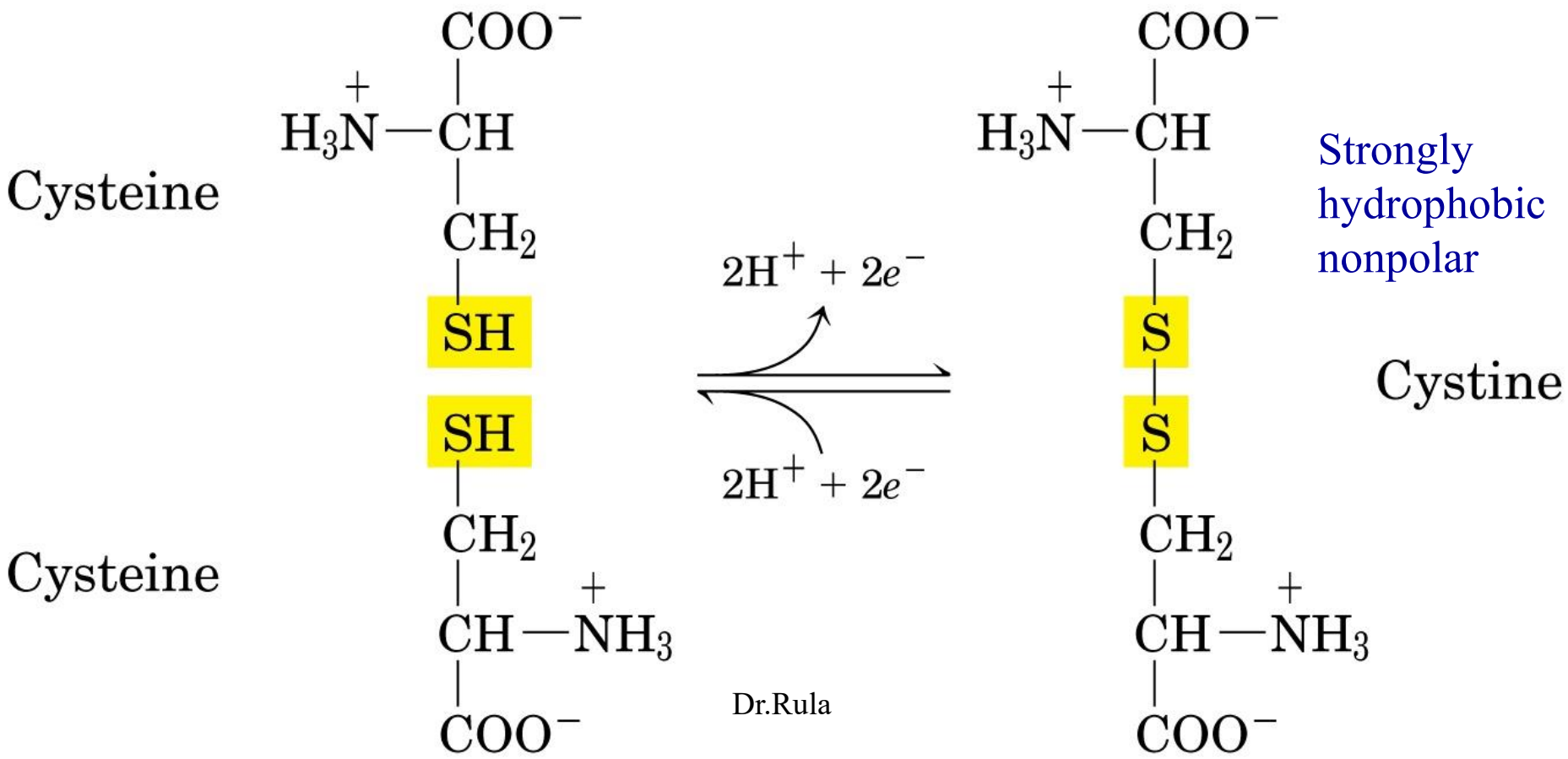


Polarity (soluble in water) form H- bond with water due to hydroxyl, sulfhydral or amide groups.

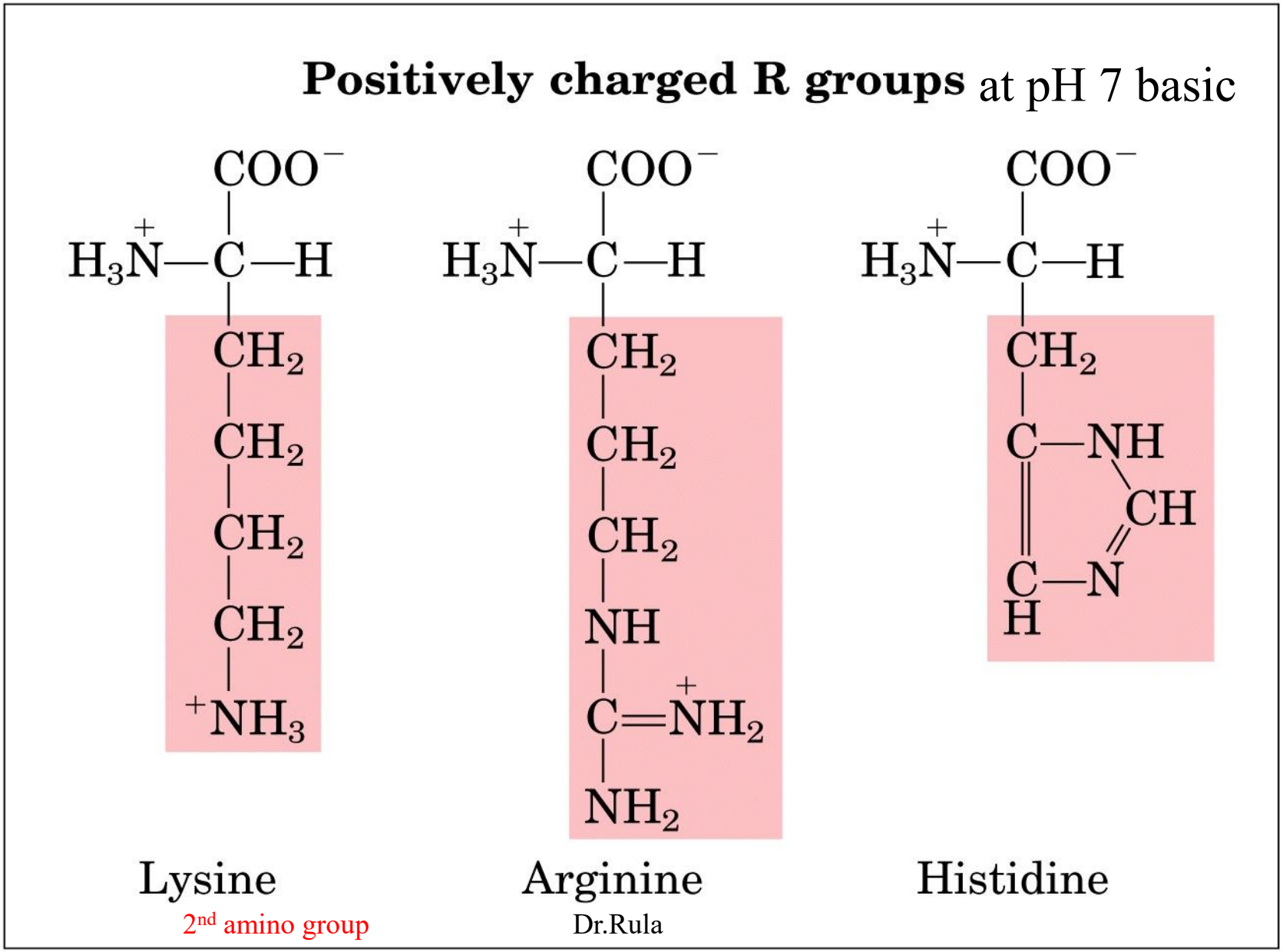


Cysteine oxidized to form a covalently linked dimeric a.a.

Cystine from a disulfide bond joining 2 Cysteine molecules.

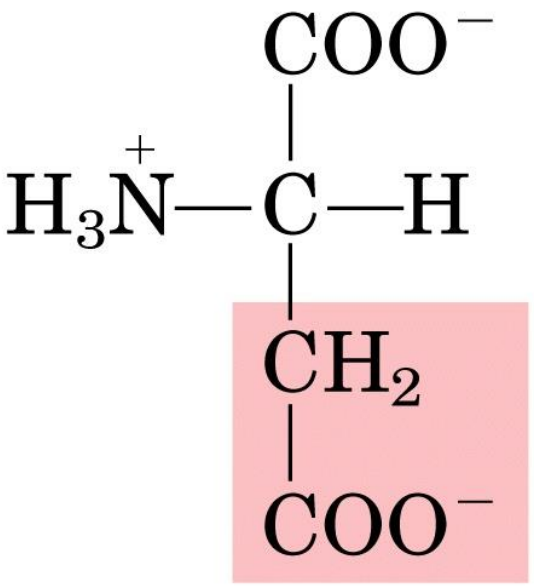


Hydrophilic R group : +ve or –ve charge.

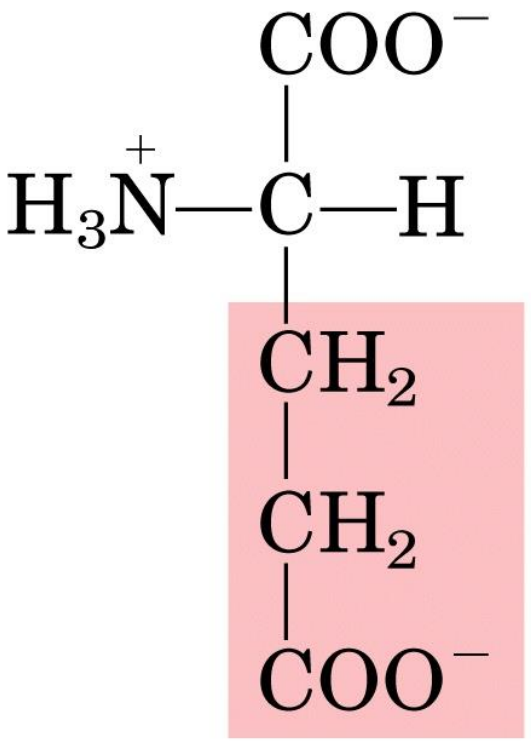


2nd amino group

Negatively charged R groups

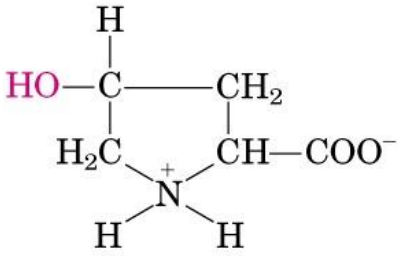


Aspartate



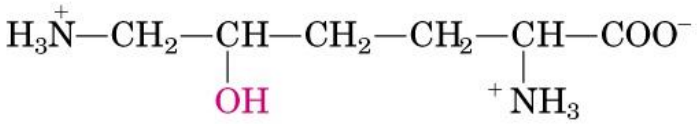
Glutamate

2) Modified a.a : uncommon protein a.a. derivatives of a.a



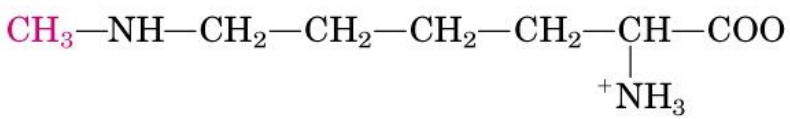
4-Hydroxyproline

Plant cell wall, collagen fibrous protein of connective tissue



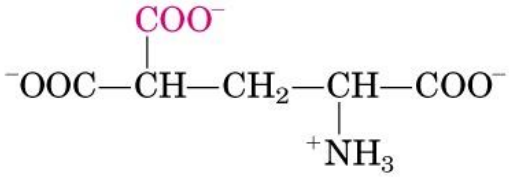
5-Hydroxylysine

Collagen fibrous protein of connective tissue



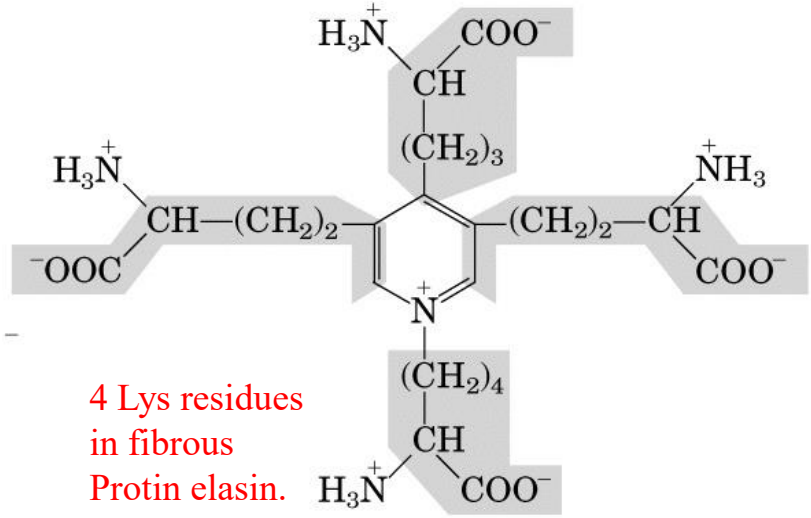
6-*N*-Methyllysine

Constituent of Myosin a contractile protein of muscle



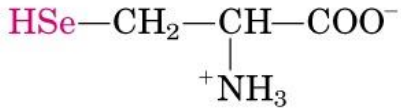
γ-Carboxyglutamate

In blood clotting protein prothrombin



4 Lys residues in fibrous Protin elasin.

Desmosine



Selenocysteine

Selenium instead of sulfur

Modified a.a during synthesis not post synthesis modification

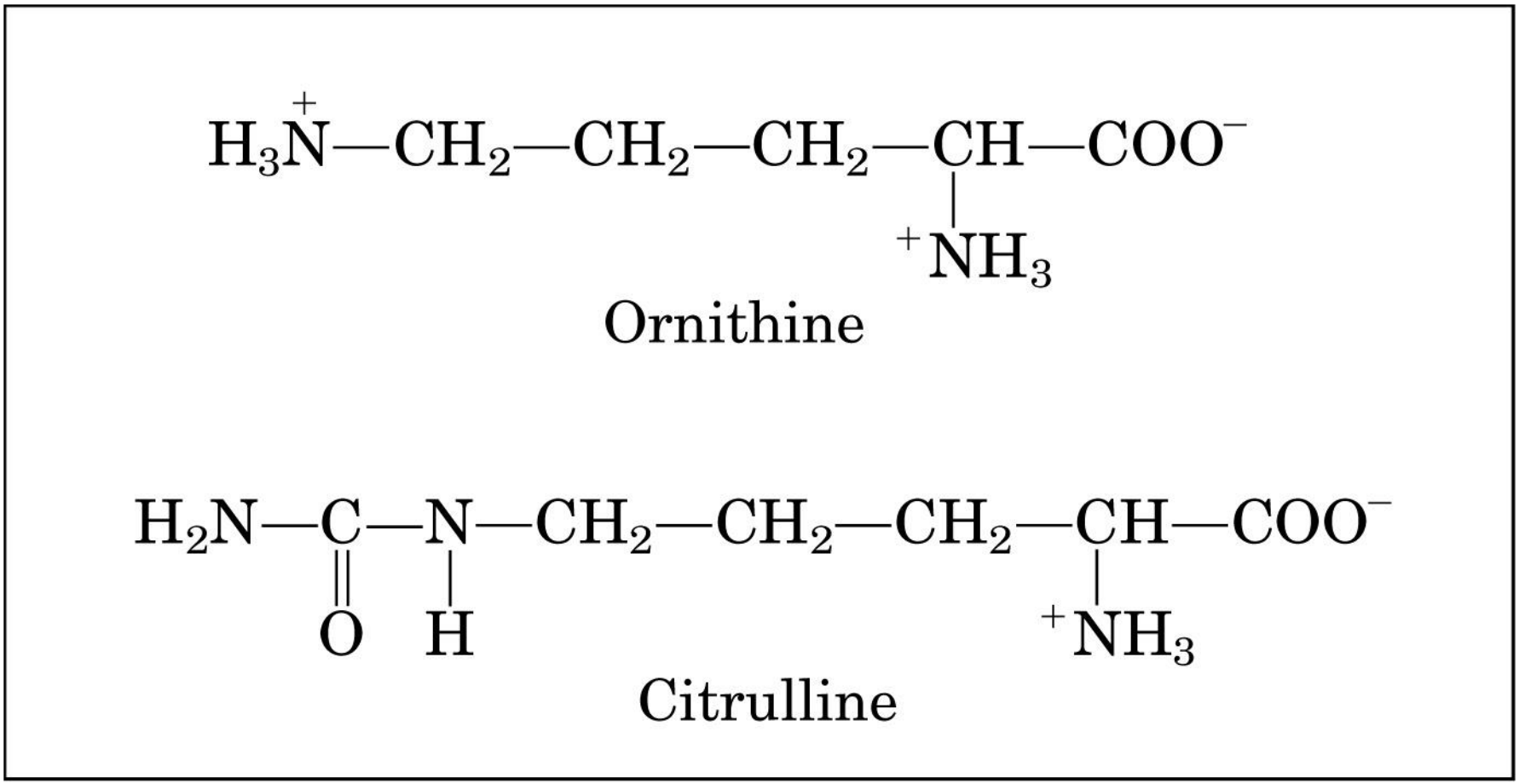
Dr.Rula

(a)

3) Non-protein a.a :

Around 300 additional a.a

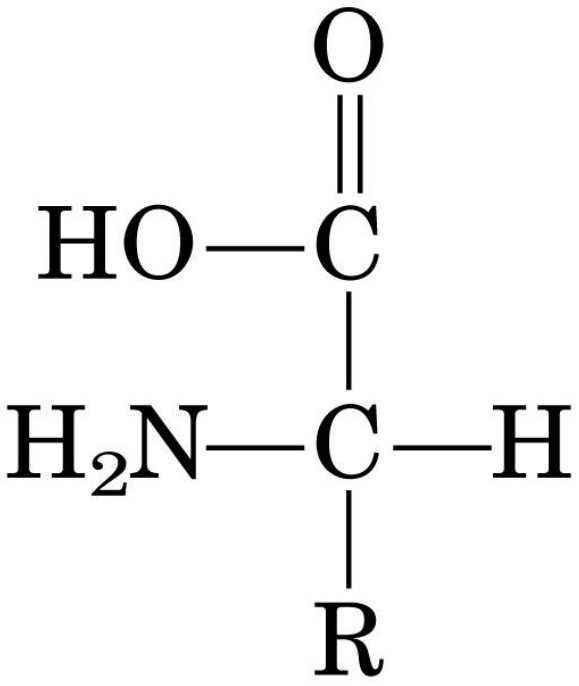
Important metabolites for pathways such as urea cycle .



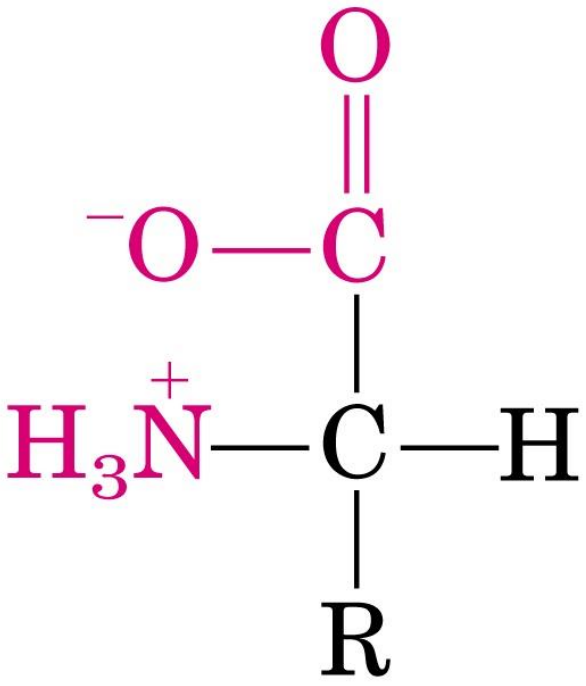
Non ionic and zwitterionic forms of a.a :predominates at neutral pH

Nonionic form does not occur in significant amounts in aqueous soln.

a.a. dissolved in water exists as dipolar ion = Zwitterionic form = hybrid ion =act as acid or base = amphoteric / ampholytes.



Nonionic form



Zwitterionic form

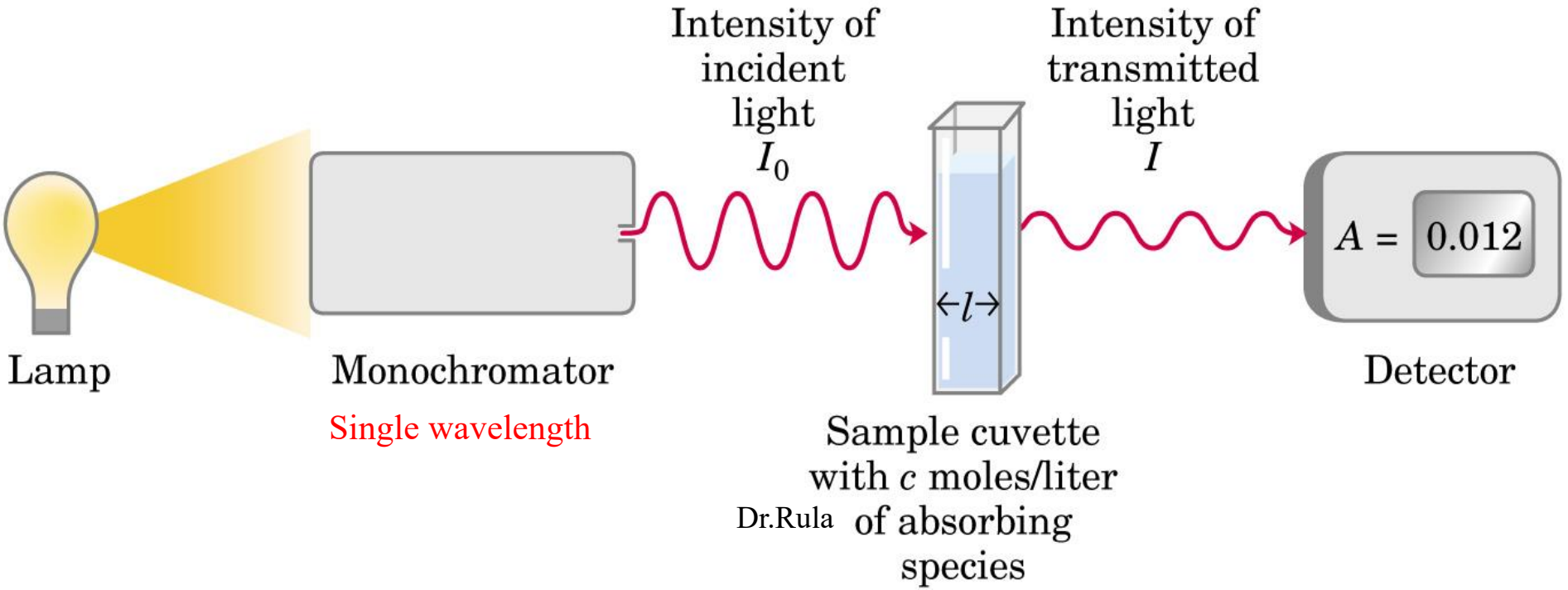
Absorption of light by molecules:

Lambert Beer law: Spectrophotometer:

The fraction of incident light absorbed by a soln at a given wavelength is related to the thickness of the absorbing layer and conc. of absorbing species.

Absorbance = A = Log Io / I = εcl

Io =intensity of incident light, I =intensity of transmitted light, ε =molar extinction coefficient , c =conc of absorbing species, l =path length



Titration of an amino acid:

1) R group non ionizable

Shaded boxes indicate 2 regions of greatest buffering power or buffering capacity.

Glycine good buffer near pH 2.34 and 9.6

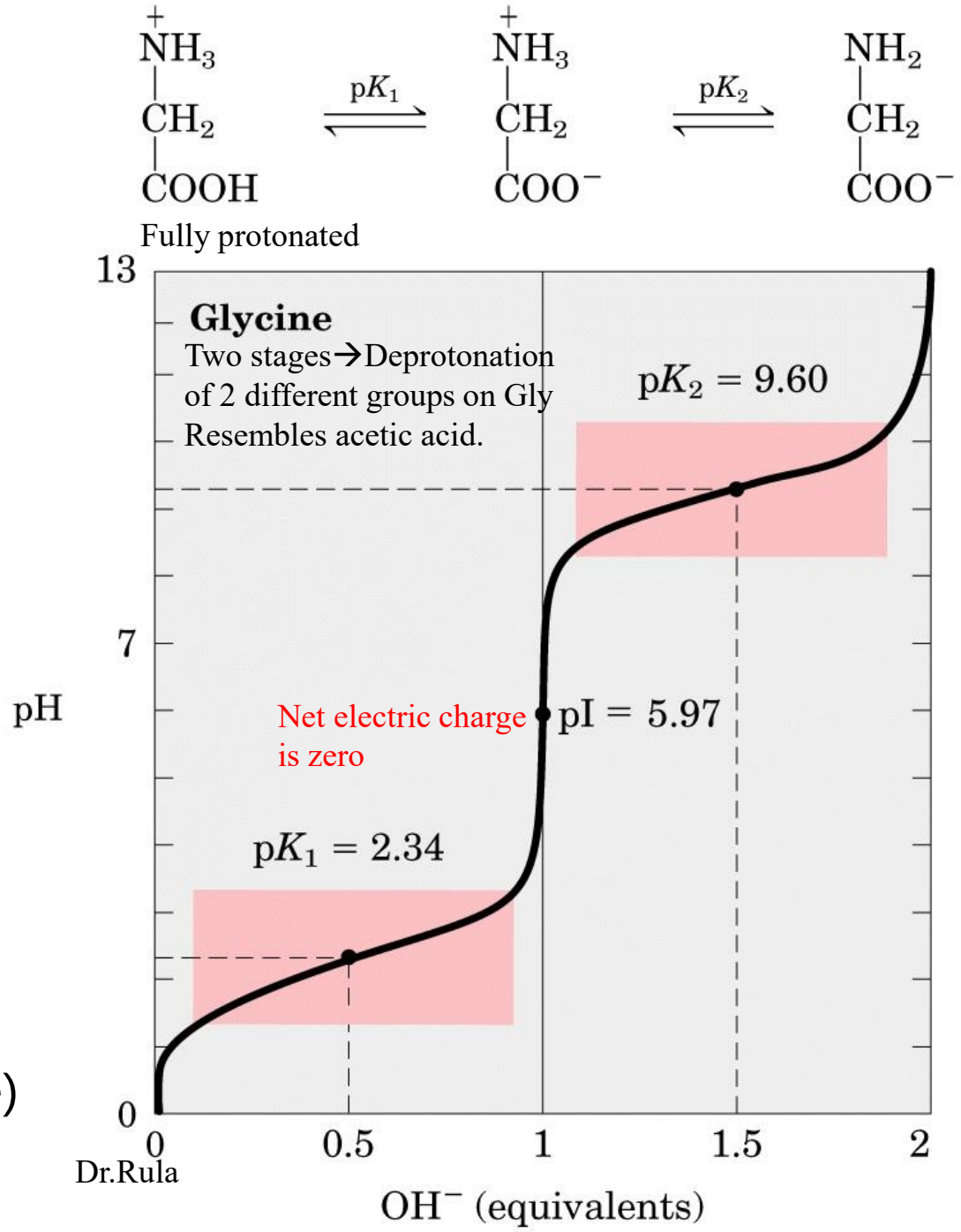
Note: glycine not a good buffer at pH of intracellular fluid or blood 7.4

PI = 0.5 (pK 1 + pK 2)

<u>In electric field</u>:

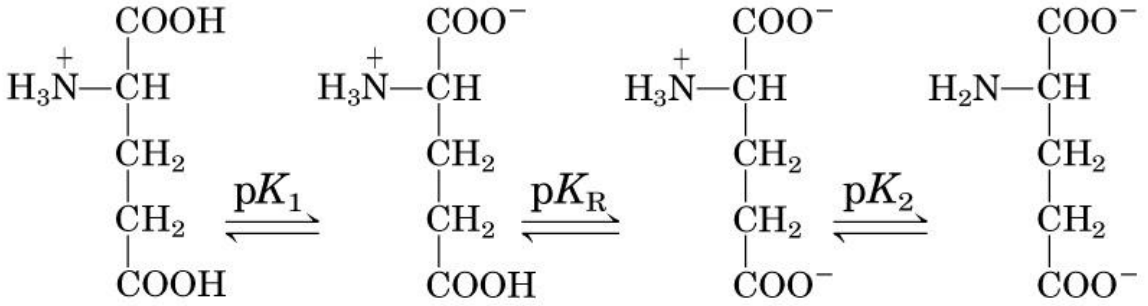
>PI towards anode (+ve electrode)

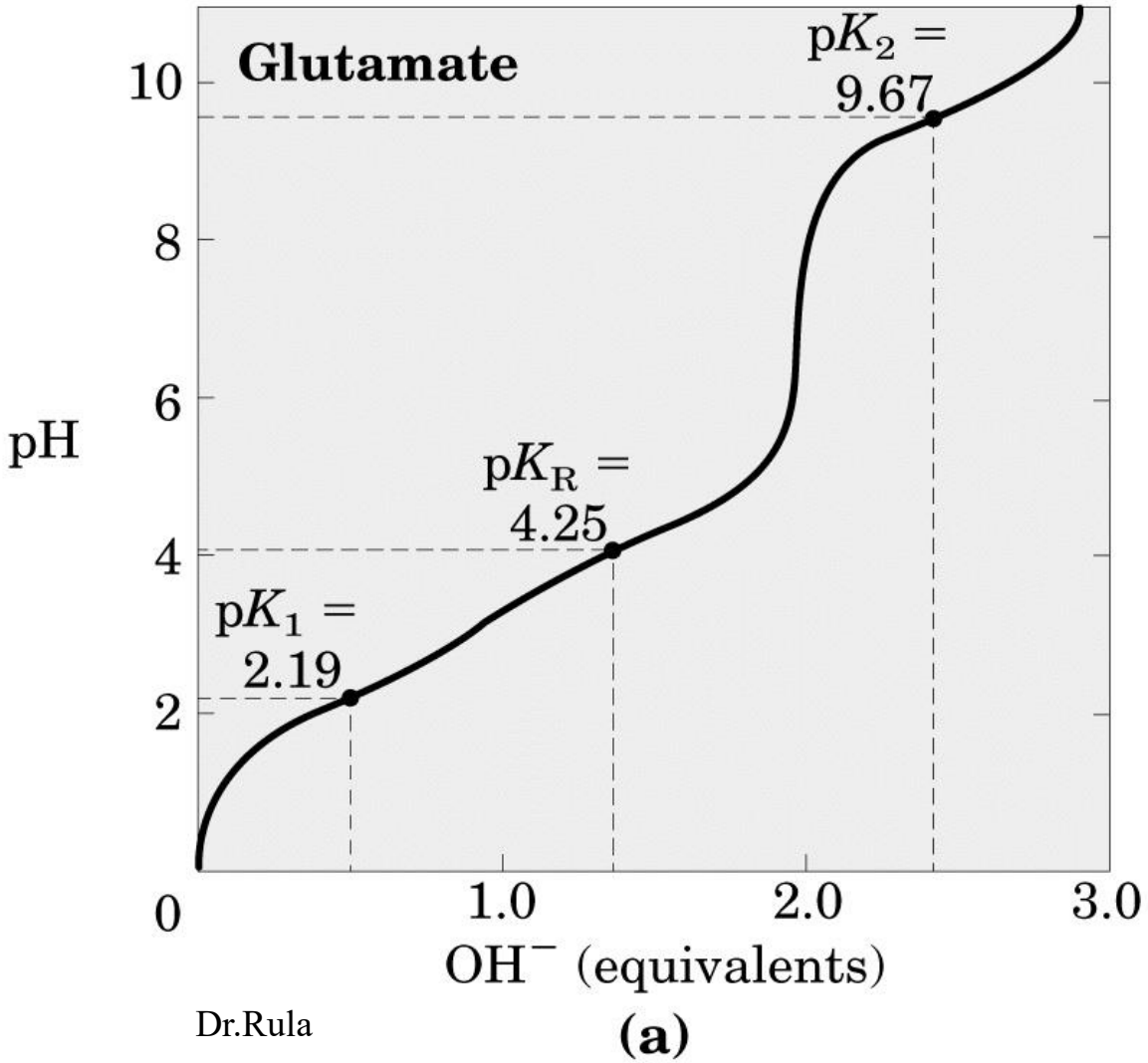
< PI towards cathode (-ve)



2) R group is ionizable:

Three stages corresponding to three possible ionization steps → 3 pKa values.

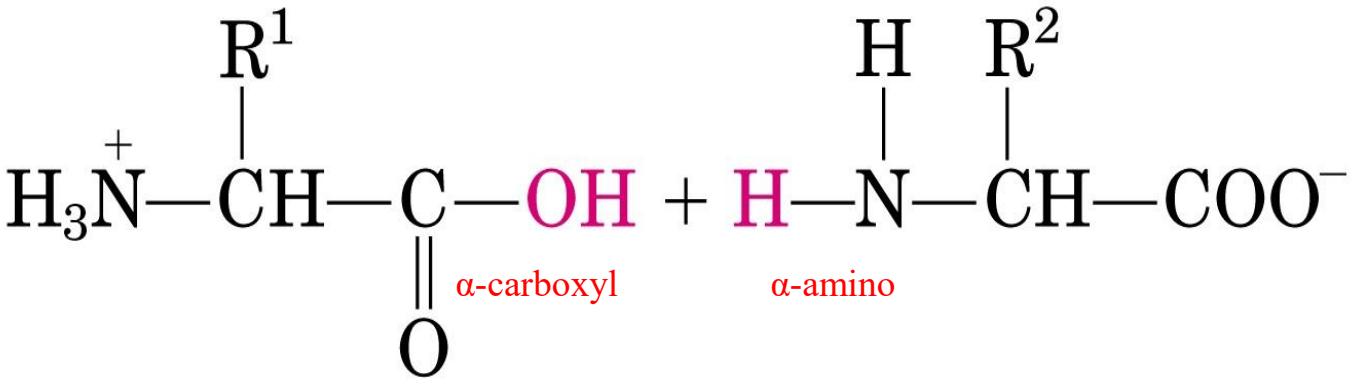




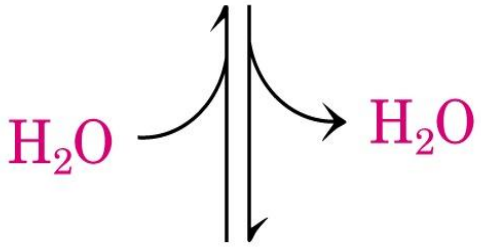
Peptides and proteins: Polymers of a.a

Range in size from 2 / 3 to thousounds of a.a

a.a. covalently joined by an amide linkage = peptide bond

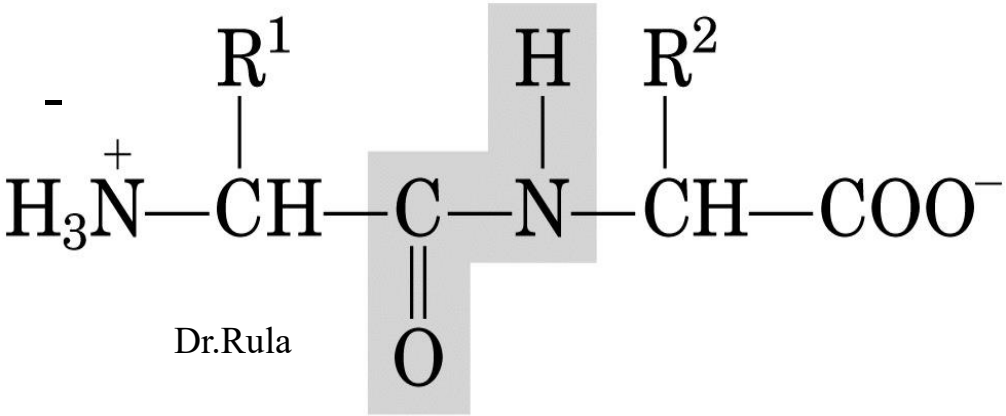


Dehydration= removal of water = condensation rxn.



Dipeptide , tripeptide, tetrapeptide,pentapeptide oligopeptide, polypeptide.

M wt <10000 =polypeptide > protein

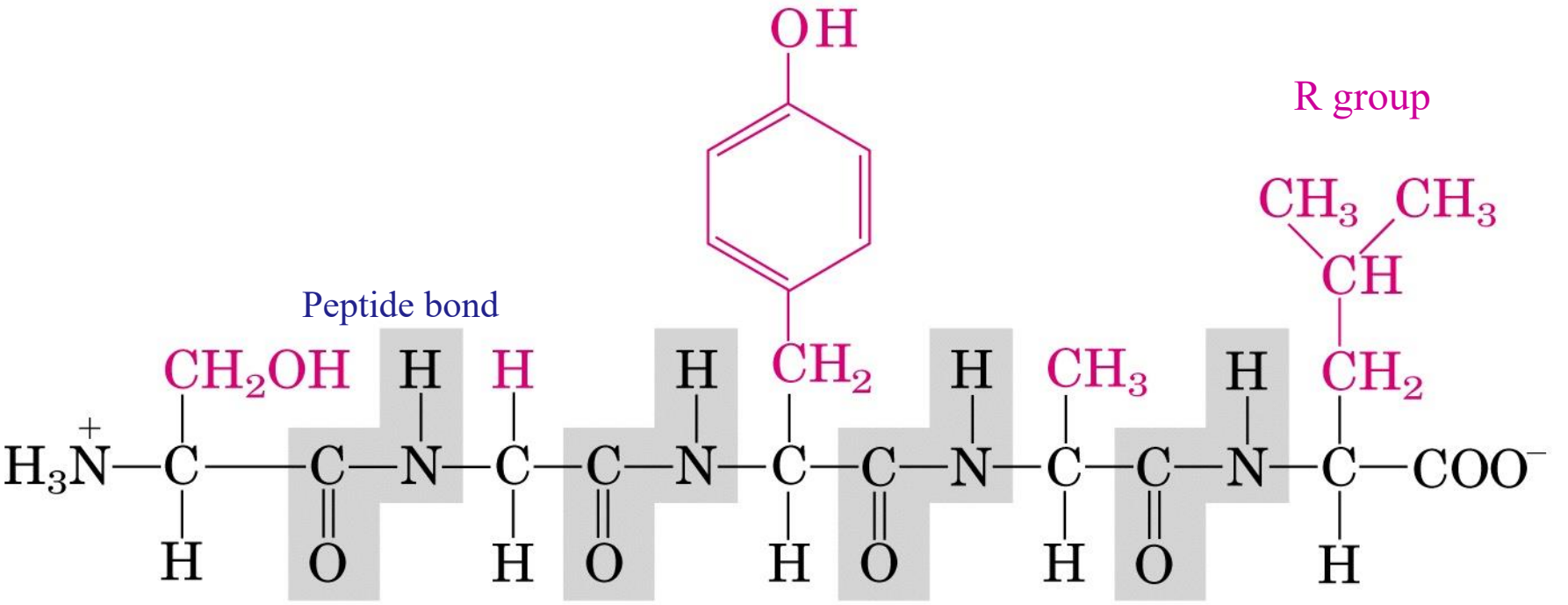


Pentapeptide:

a.a. unit in a peptide = residue

Ser-Gly-Tyr-Ala-Leu or serylglycyltyrosylalanylleucine

By convention left → right .

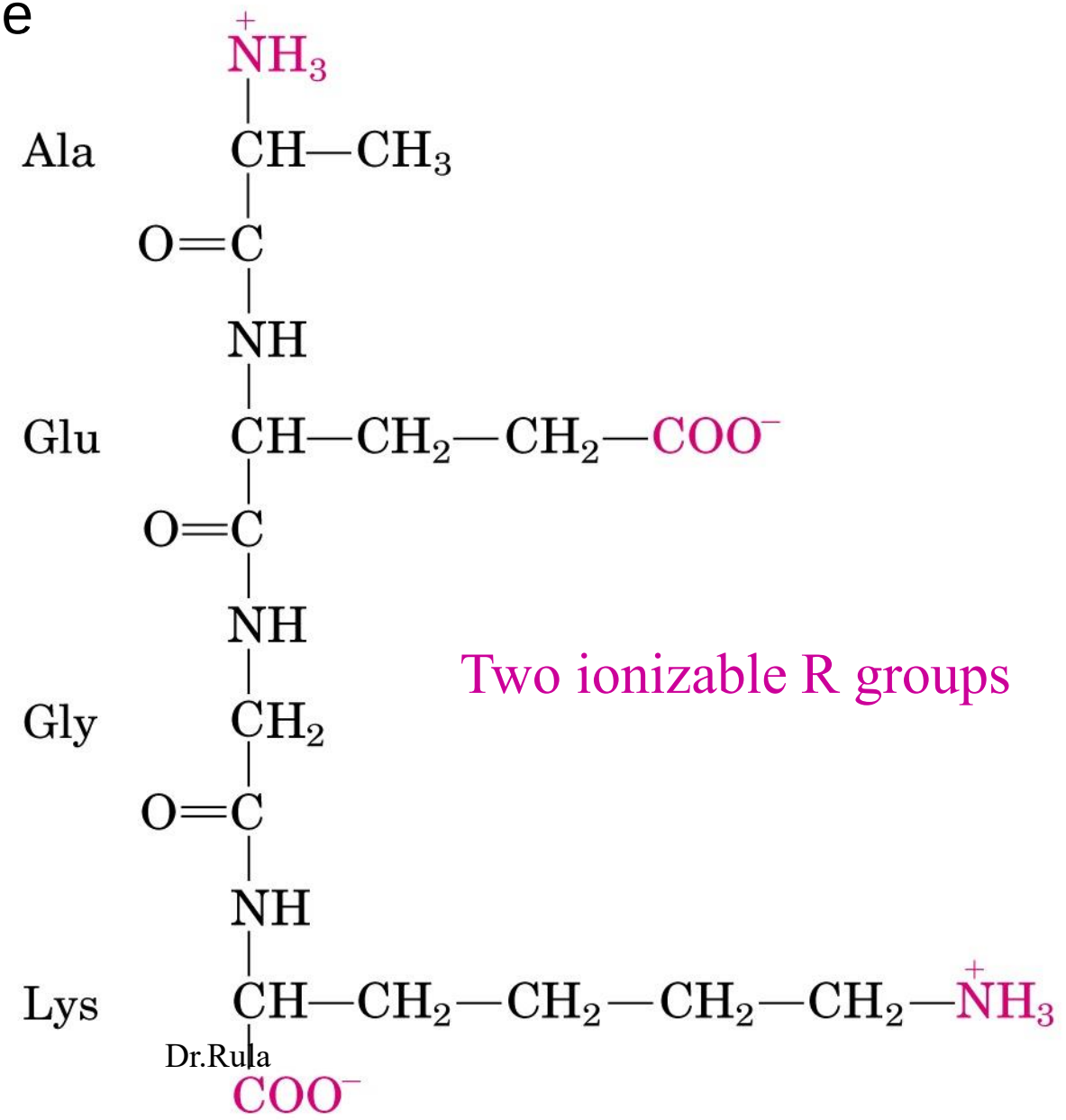


Tetrapeptide:

Alanylglutamylglycyllysine

Peptides have only one free amino termial and one free carboxyl group.

Acid - base behavior of a peptide depend on the R groups and free amino free carboxyl ends (not nonterminal ends).



Two ionizable R groups

Many small peptides exert their effect at low conc.

1) Hormones:

Oxytocin (9 a.a) → uterine contraction , milk secretion.

Bradykinin (9 a.a) → inhibits tissue inflamation

Some Hormones are oligopeptides:
insulin two chains 30+21 a.a,
Glucagon 29 a.a

2) Toxins : mushroom poisons.

3) Antibiotics.

Length and number of polypeptide chains vary from one protein to another.

Single polypeptide chain or multisubunit protein (2/more polypeptides identical/different associated non covalently).

If at least 2 identical, protein called oligomeric, the identical unit called protomer.

Hemoglobin 4 polypeptide subunits 2α 2β = tetramer/ dimer of αβ protemer.

Insulin 2 polypeptide chains (disulfide bond) not subunits.

table 5–2

Molecular Data on Some Proteins

	Molecular weight	Number of residues	Number of polypeptide chains
Cytochrome *c* (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	21,600	241	3
Chymotrypsinogen (bovine)	22,000	245	1
Hemoglobin (human)*	64,500	574	4
Serum albumin (human)	68,500	609	1
Hexokinase (yeast)	102,000	972	2
RNA polymerase (*E. coli*)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (*E. coli*)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

Hydrolysis of peptides/proteins with acids yield the free a.a.

Some a.a occur once or not at all in a certain protein

table 5–3

Amino Acid Composition of Two Proteins*

Amino acid	Number of residues per molecule of protein: Bovine cytochrome *c*	Bovine chymotrypsinogen
Ala	6	22
Arg	2	4
Asn	5	15
Asp	3	8
Cys	2	10
Gln	3	10
Glu	9	5
Gly	14	23
His	3	2
Ile	6	10
Leu	6	19
Lys	18	14
Met	2	2
Phe	4	6
Pro	4	9
Ser	1	28
Thr	8	23
Trp	1	8
Tyr	4	4
Val	3	23
Total	104	245

*Note that standard procedures for the acid hydrolysis of proteins convert Asn and Gln to Asp and Glu, respectively. In addition, Trp is destroyed. Special procedures must be employed to determine the amounts of these amino acids.

Conjugated proteins:

proteins that contain chemical groups other than a.a.

Prosthetic group: non-amino acid part of the conjugated protein.

Conjugated proteins classified according to the prosthetic group.

table 5–4

Conjugated Proteins

Class	Prosthetic group(s)	Example
Lipoproteins	Lipids	β_1-Lipoprotein of blood
Glycoproteins	Carbohydrates	Immunoglobulin G
Phosphoproteins	Phosphate groups	Casein of milk
Hemoproteins	Heme (iron porphyrin)	Hemoglobin
Flavoproteins	Flavin nucleotides	Succinate dehydrogenase
Metalloproteins	Iron	Ferritin
	Zinc	Alcohol dehydrogenase
	Calcium	Calmodulin
	Molybdenum	Dinitrogenase
	Copper	Plastocyanin

Several levels of protein structure:

Primary structure is the sequence of a.a linked together by peptide bonds and includes any disulfide bonds.