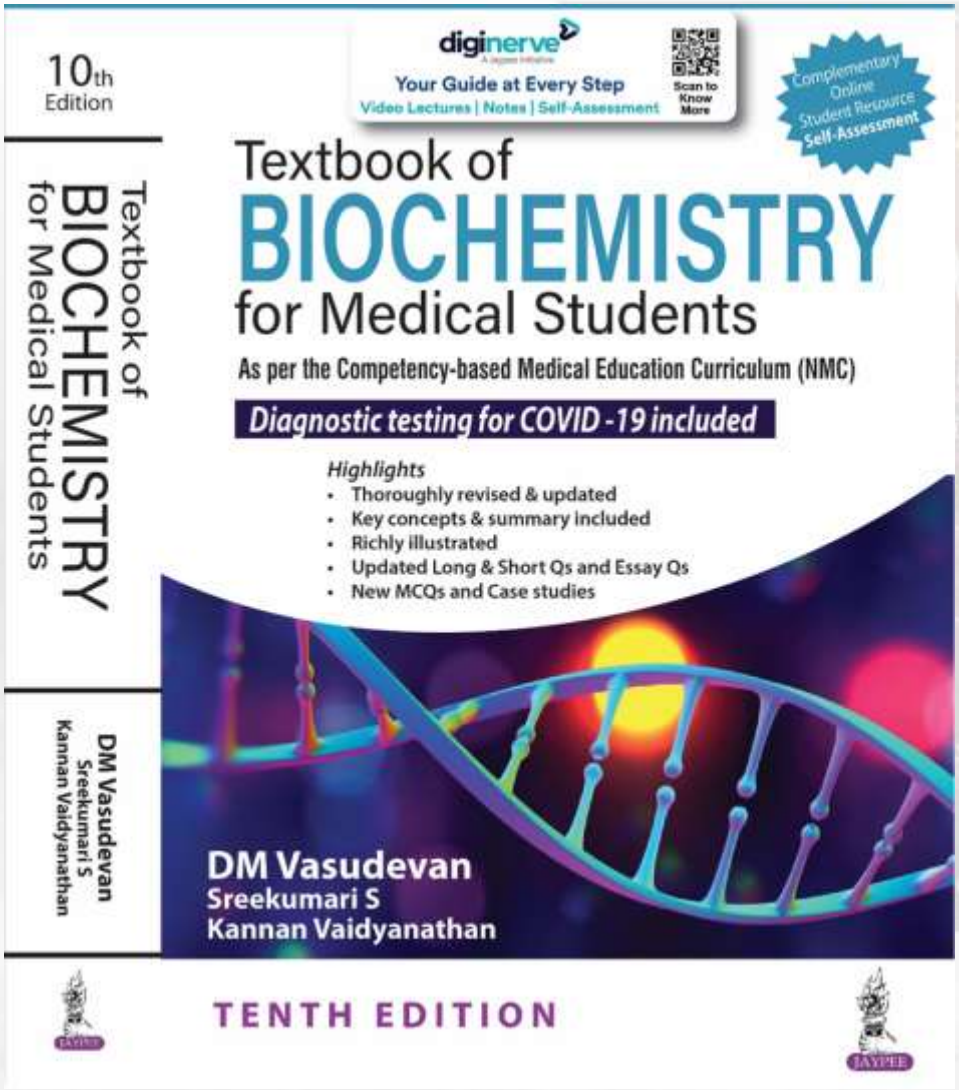
Chapter 3A:

Chemistry of Amino Acids

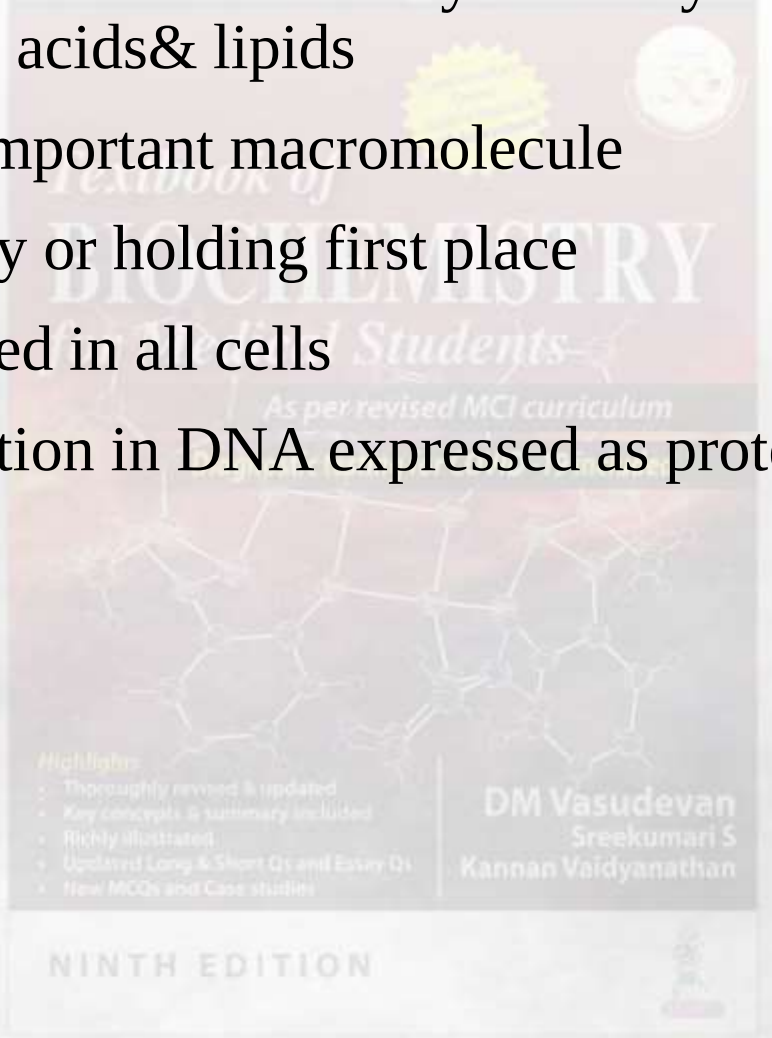


Textbook of
BIOCHEMISTRY
for Medical Students

By DM Vasudevan, *et al.*

TENTH EDITION

- Major macromolecules in the body: carbohydrates, proteins, nucleic acids& lipids
- Proteins- most important macromolecule
- Proteios- primary or holding first place
- Widely distributed in all cells
- Genetic information in DNA expressed as proteins



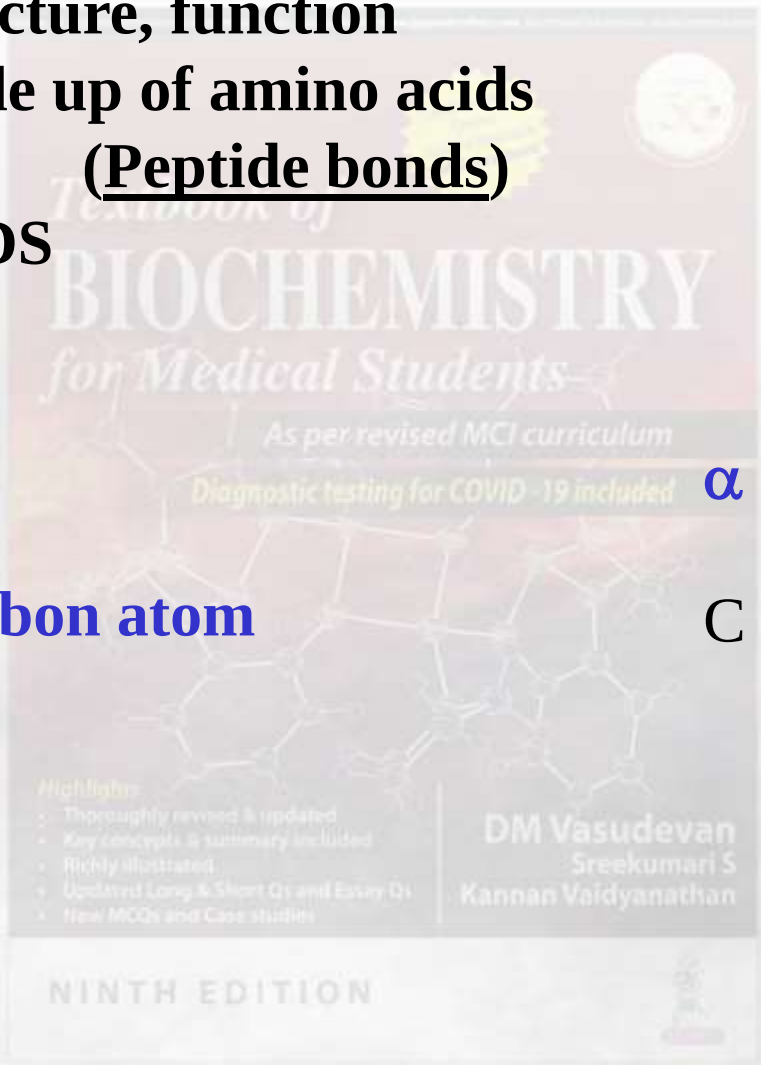
Amino Acids and Proteins

PROTEINS: structure, function

PROTEINS: made up of amino acids

(Peptide bonds)

20 AMINO ACIDS



COOH
|
CH--NH2 **α carbon atom**
|
R

α amino acids

C , H, O, **N**
16%

Classificatiion of Amino Acids

I. Based on Structure

II. Based on side chain characters

III. Based on Metabolic fate

IV. Based on nutrutional requirement

Amino Acids Classification Based on Structure

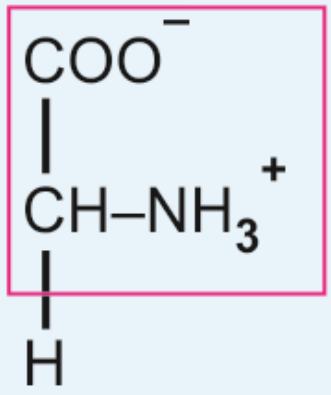
1. **ALIPHATIC AMINO ACIDS**
   - A. Mono Amino Mono Carboxylic Acids (Neutral)
   - B. Mono Amino Di Carboxylic Acids (Acidic)
   - C. Di Amino Mono Carboxylic Acids (Basic)
2. **AROMATIC AMINO ACIDS**
3. **HETEROCYCLIC AMINO ACIDS**
4. **IMINO ACID**
5. **DERIVED AMINO ACIDS**

Amino Acids Classification Based on Structure

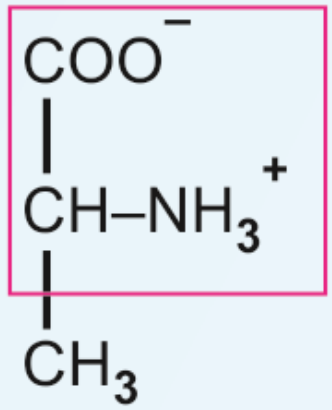
1. ALIPHATIC AMINO ACIDS

A. MONO AMINO MONOCARBOXYLIC ACIDS

a. Simple amino acids



Glycine
Gly; G

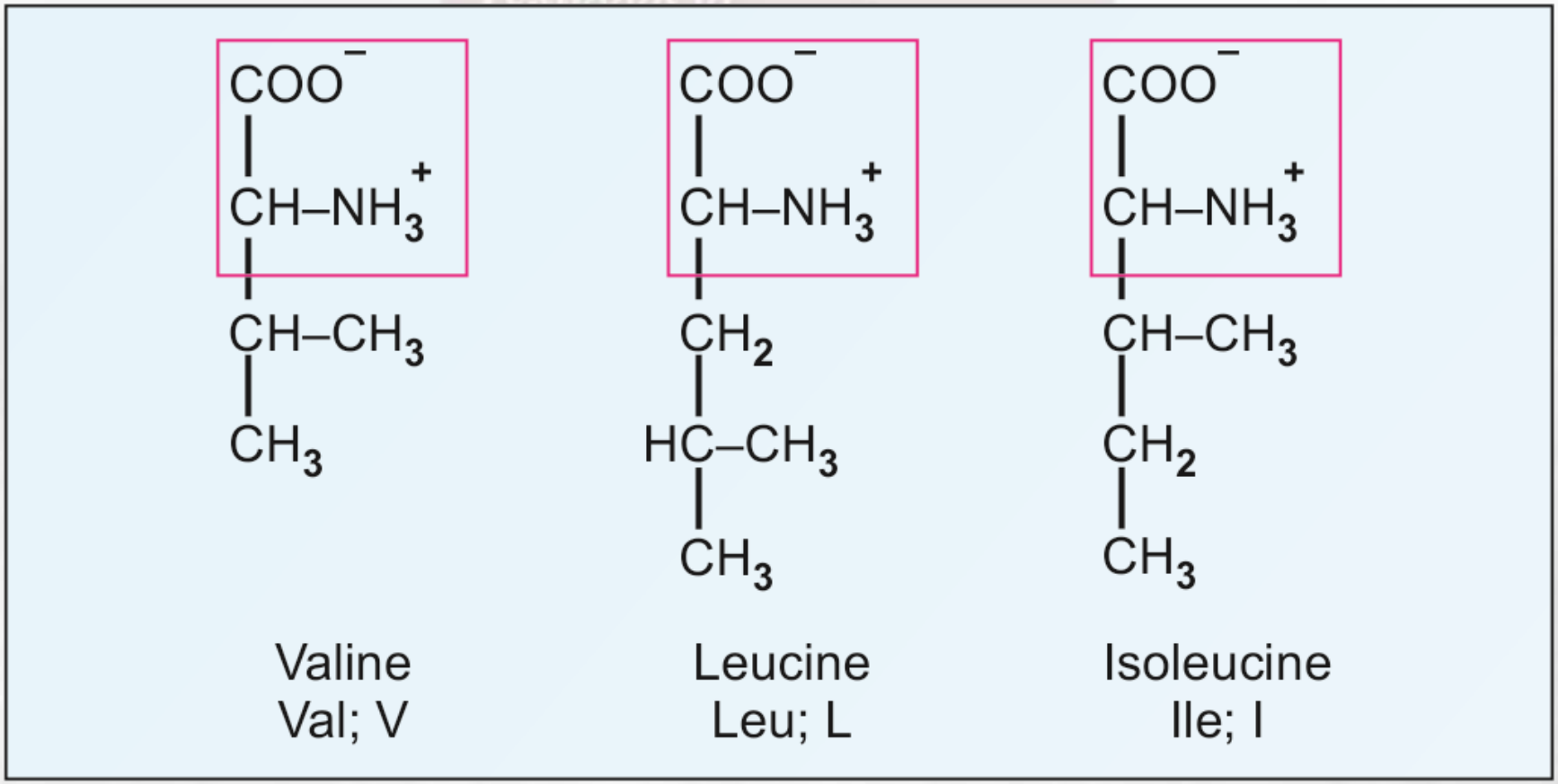


Alanine
Ala; A

A. MONO AMINO MONO CARBOXYLIC ACIDS

a. Simple Amino Acids

b. Branched Chain Amino Acids (BCA)

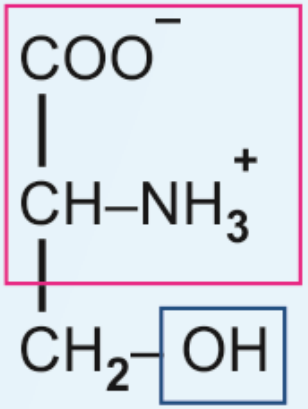


A. MONO AMINO MONO CARBOXYLIC ACIDS

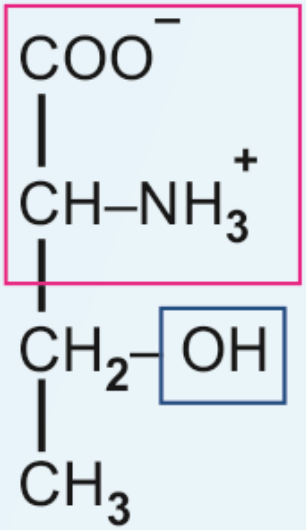
a. Simple Amino Acids

b. Branched Chain Amino Acids (BCA)

c. Hydroxy Amino Acids



Serine; Ser; S



Threonine; Thr; T

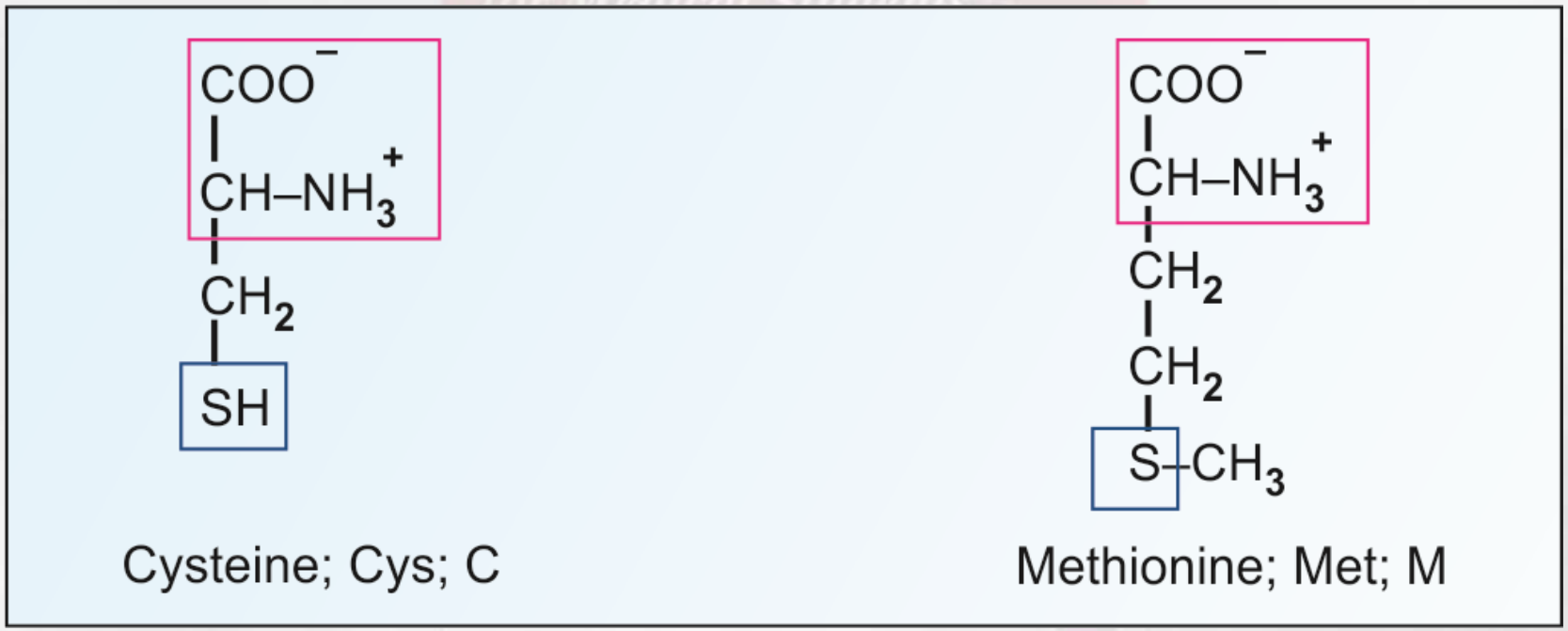
A. MONO AMINO MONO CARBOXYLIC ACIDS

(a) Simple Amino Acids

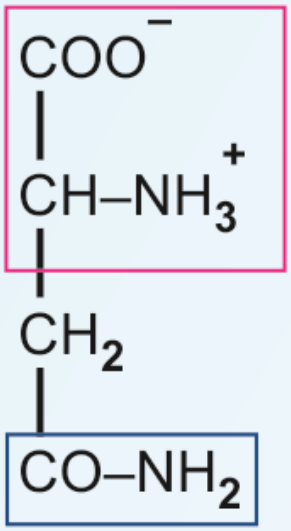
(b) Branched Chain Amino Acids (BCA)

(c) Hydroxy Amino Acids

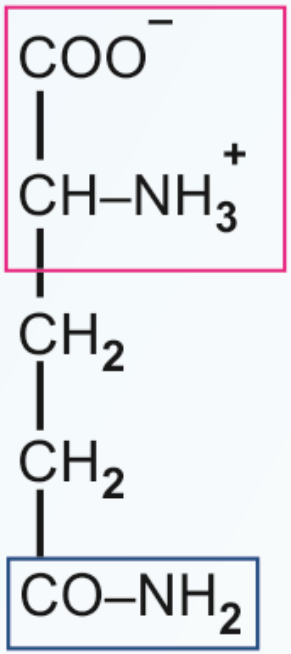
(d) **Sulphur Containing amino acids**



A (e) AMINO ACIDS WITH AMIDE GROUP NEUTRAL

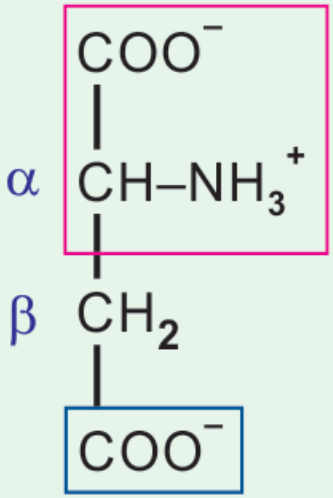


Asparagine; Asn; N

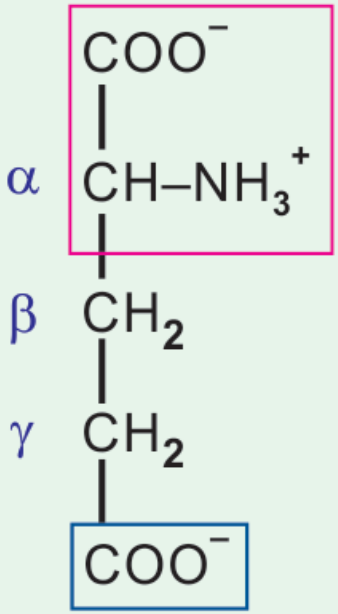


Glutamine; Gln; Q

B. MONO AMINO DI CARBOXYLIC ACIDS ACIDIC



Aspartic acid; Asp; D
(β-carboxyl group)



Glutamic acid; Glu; E
(γ-carboxyl group)

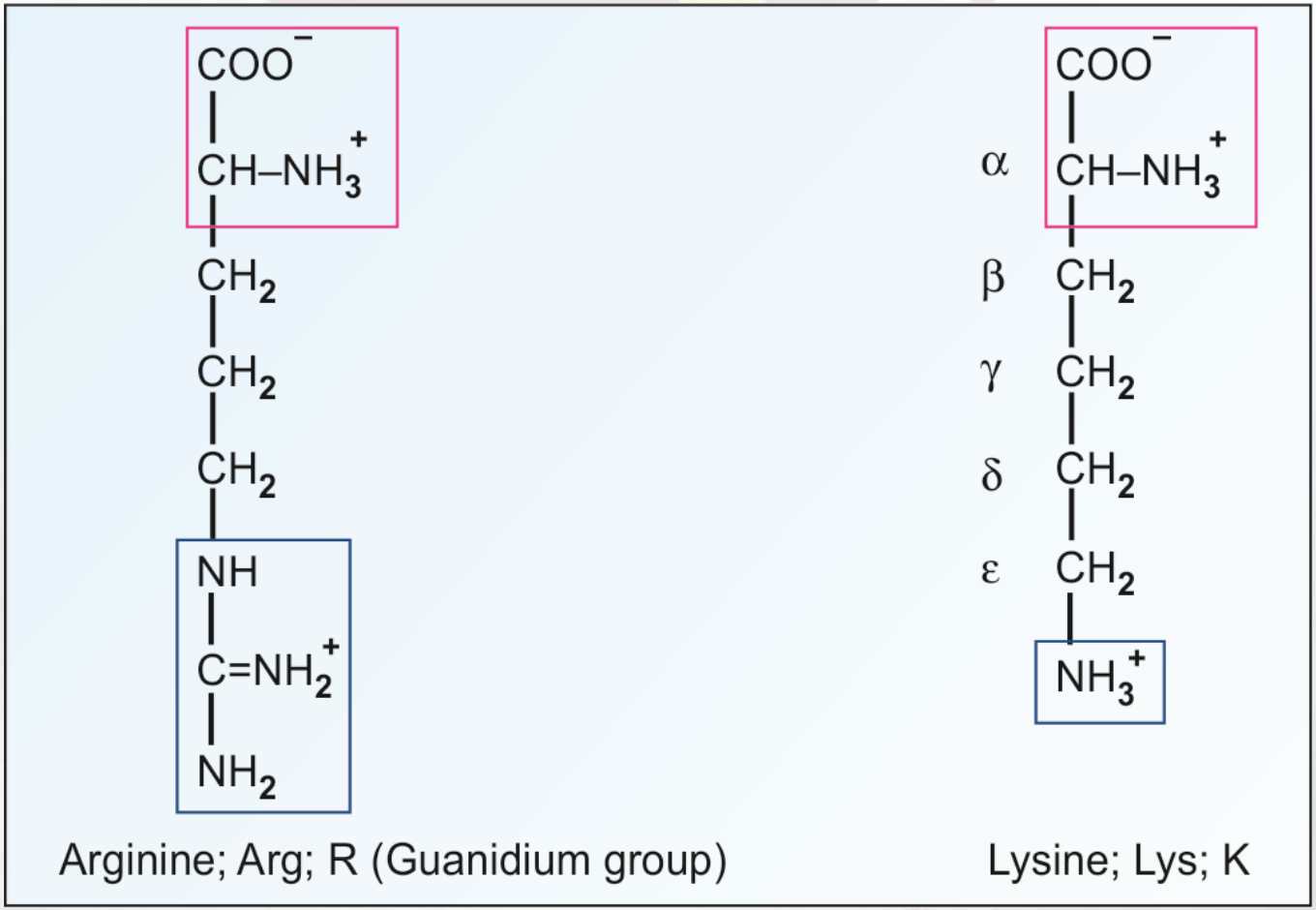
1. Aliphatic amino acids

A. Mono amino mono carboxylic acids (neutral)

B. Mono amino dicarboxylic acids (acidic)

C. Di amino mono carboxylic acids (basic)

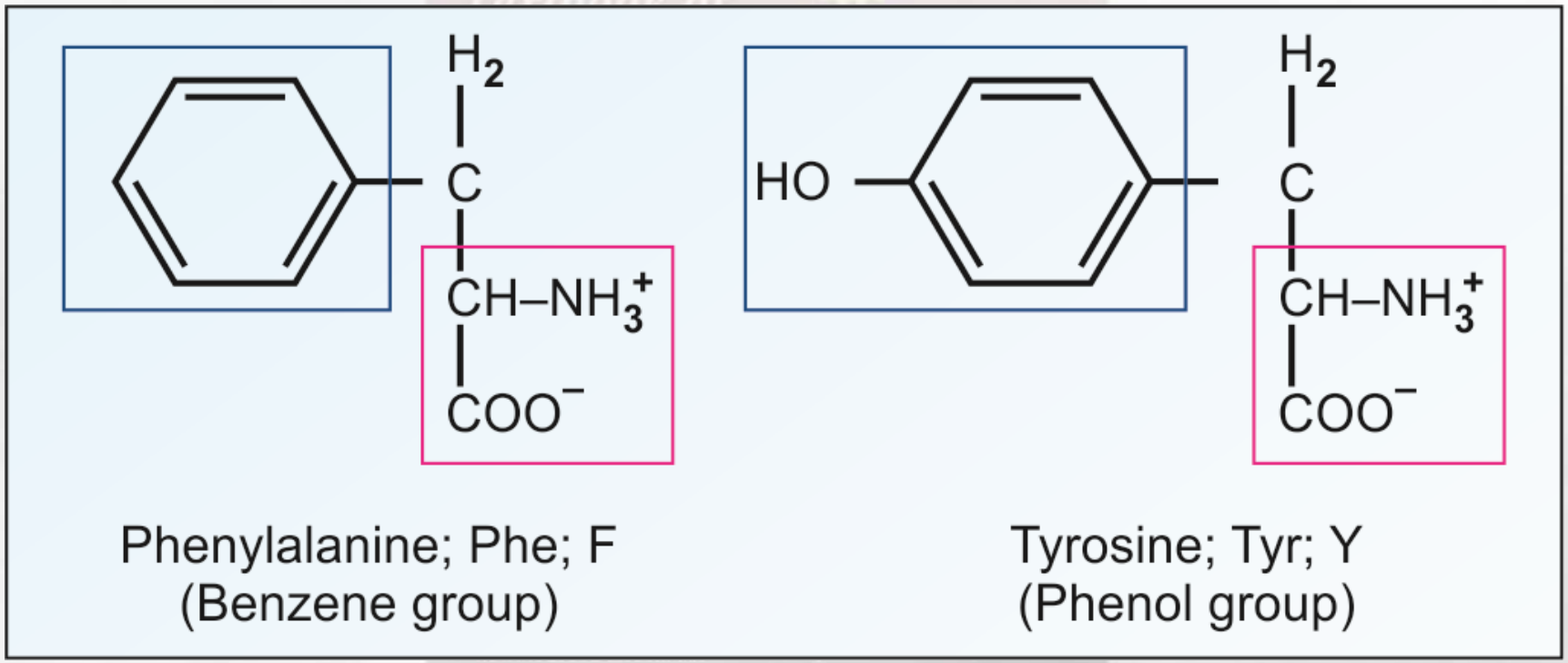
1. C. DI AMINO MONO CARBOXYLIC ACIDS



Arginine; Arg; R (Guanidium group)

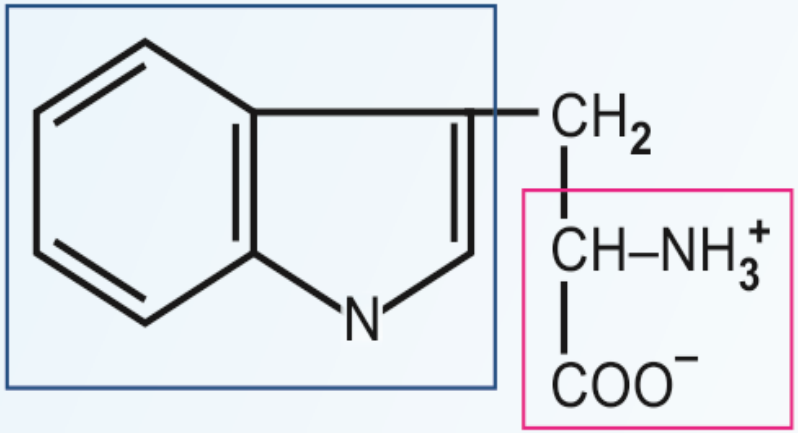
Lysine; Lys; K

1. **Aliphatic amino acids**
2. **AROMATIC AMINO ACIDS**



1. **Aliphatic amino acids**
2. **Aromatic amino acids**
3. **HETEROCYCLIC AMINO ACIDS**

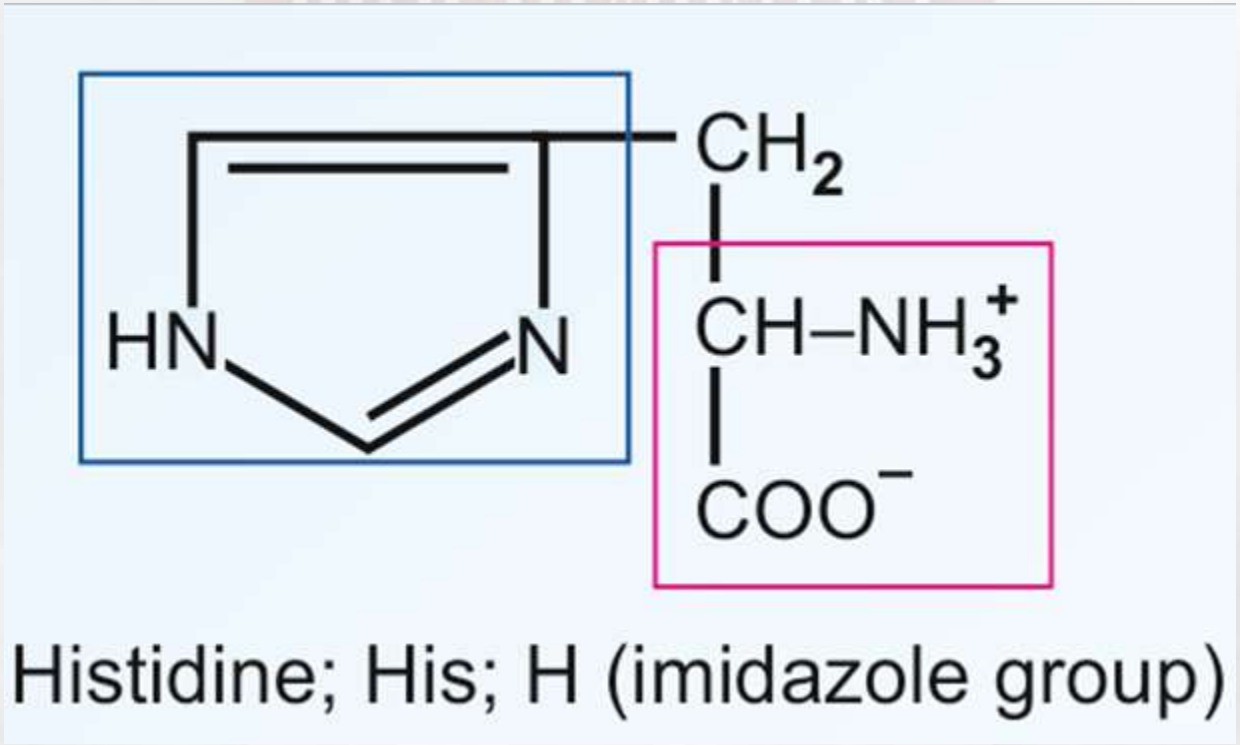
Indole ring



TRYPTOPHAN TRP; W

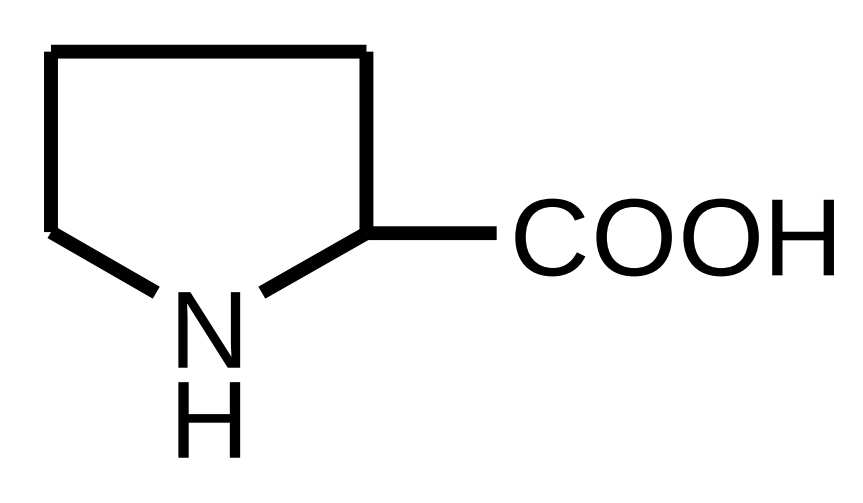
(Heaviest amino acid)

1. **Aliphatic amino acids**
2. **Aromatic amino acids**
3. **HETEROCYCLIC AMINO ACIDS**



Histidine; His; H (imidazole group)

1. **Aliphatic amino acids**
2. **Aromatic Amino Acids**
3. **Heterocyclic amino acids**
4. **I M I N O A C I D**



20. <u>PROLINE</u> PRO; P

PYRROLIDINE GROUP

1. Aliphatic amino acids
2. Aromatic Amino Acids
3. Heterocyclic amino acids
4. Imino acid
5. DERIVED AMINO ACIDS

A. PRESENT IN PROTEINS
B. NOT PRESENT IN PROTEINS
C. NON-ALPHA AMINO ACIDS

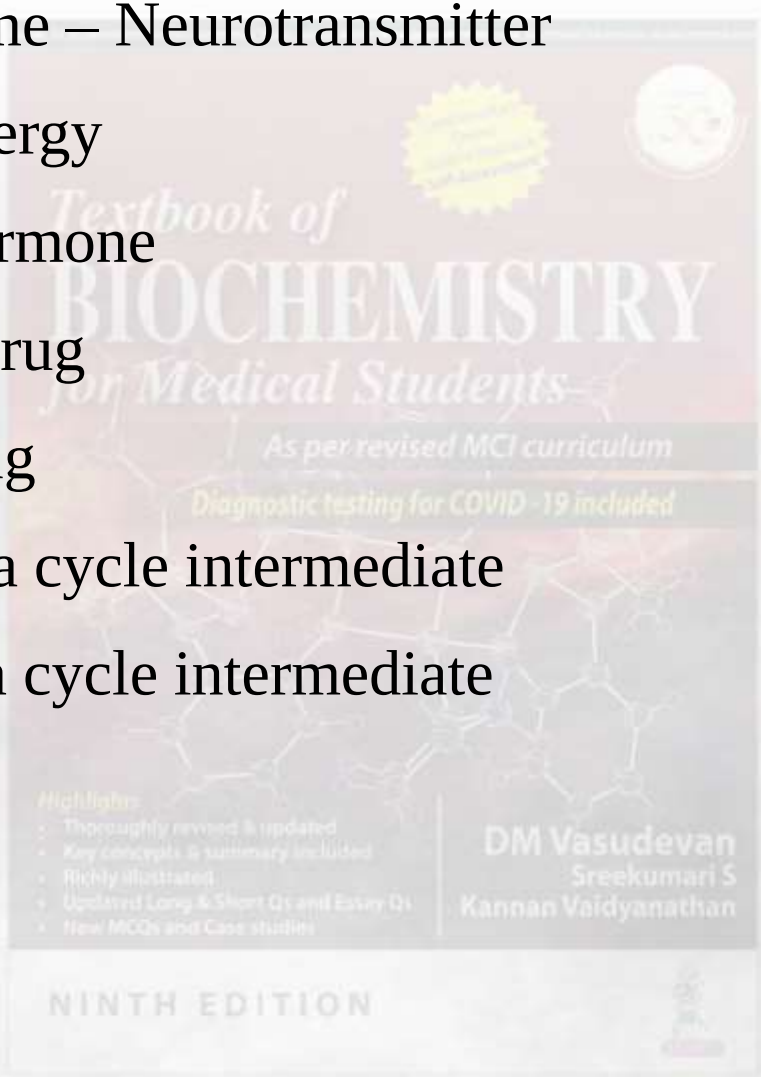
Derived amino acids

- Found in proteins –
  - Hydroxy proline, hydroxy lysine (Collagen)
  - Gamma carboxy glutamic acid (Clotting)
  - Methylated and acetylated proteins (Ribosomal proteins and histones)
- Not found in proteins (Non-protein amino acids)
  - Ornithine, citrulline – Urea cycle
  - Homocysteine – Sulphur containing amino acid
- Non-alpha amino acids
  - GABA – Derived from glutamic acid
  - Beta alanine (seen in CoA)

1. **ALIPHATIC AMINO ACIDS**
   - **A. Mono Amino Mono Carboxylic Acids**
     - **a. Simple amino acids:** G, A
     - **b. Branched Chain amino acids:** V, L, I
     - **c. Hydroxy amino acids:** S, T
     - **d. Sulphur containing amino acids:** C, M
     - **e. Amino acids with amide group:** N, Q
   - **B. Mono Amino Di Carboxylic Acids:** D, E
   - **C. Di Amino Mono Carboxylic Acids:** R, K
2. **AROMATIC AMINO ACIDS:** F, Y
3. **HETEROCYCLIC AMINO ACIDS :** W, H
4. **IMINO ACID :** P
5. **DERIVED AMINO ACIDS**

Derived Amino Acids

- GABA, dopamine – Neurotransmitter
- Histamine – Allergy
- Thyroxine – Hormone
- Cycloserine – Drug
- Azaserine – Drug
- Ornithine – Urea cycle intermediate
- Citrulline - Urea cycle intermediate



Special Groups in Amino Acids

Arginine	**guanidinium group**
Phenylalanine	**benzene group**
Tyrosine	**phenol**
Tryptophan	**indole**
Histidine	**imidazole**

Classification of amino acids

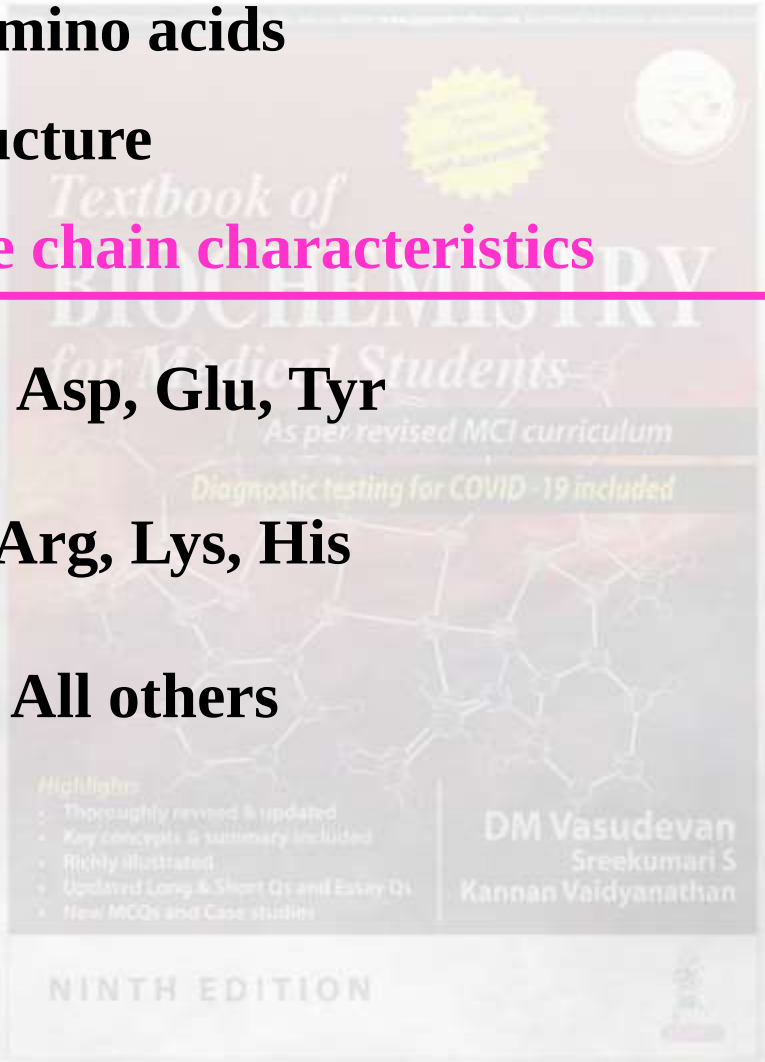
I. based on Structure

II. Based on Side chain characteristics

ACIDIC : Asp, Glu, Tyr

BASIC : Arg, Lys, His

NEUTRAL : All others



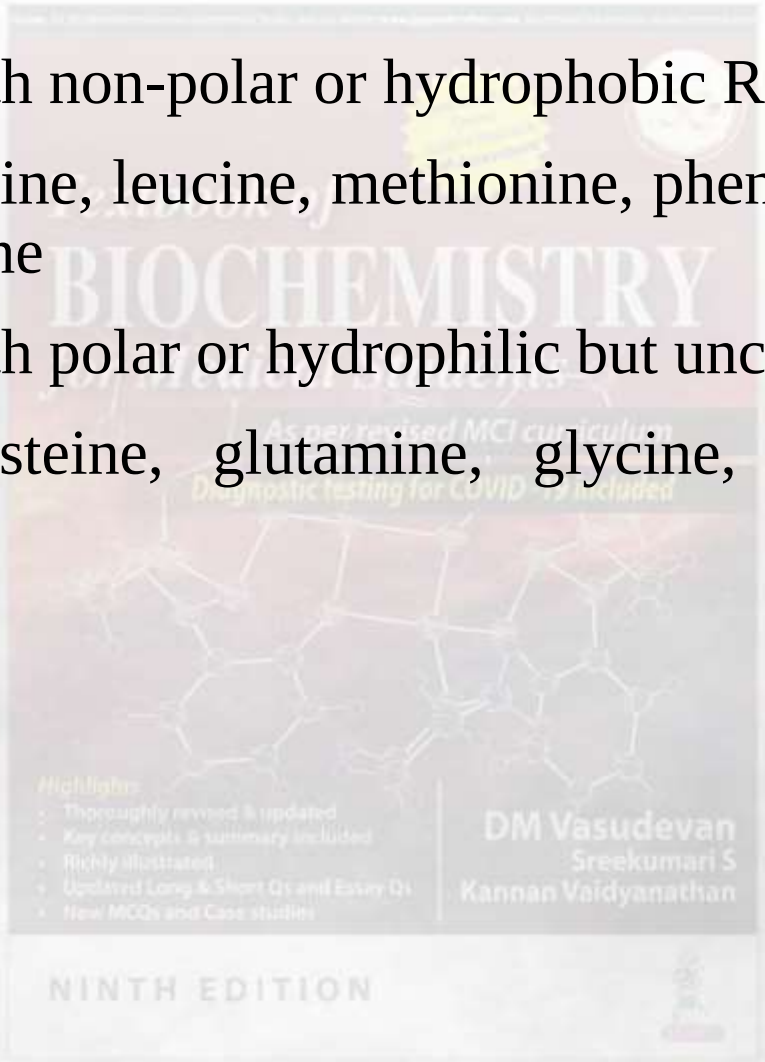
Classification of A. As Based on Polarity of Their R Groups

- Amino acids with non-polar or hydrophobic R groups :

  Alanine, isoleucine, leucine, methionine, phenyl alanine, proline, tryptophan, valine

- Amino acids with polar or hydrophilic but uncharged R groups:

  Asparagine, cysteine, glutamine, glycine, serine, threonine, tyrosine



- Polar amino acids with charged R groups:
  - Negatively charged R groups present in
    - aspartic acid
    - glutamic acid
  - Positively charged R groups present in
    - arginine
    - histidine
    - lysine

Classification of amino acids

I. based on Structure

II. Based on Side chain characteristics

III. Based on Metabolic Fate

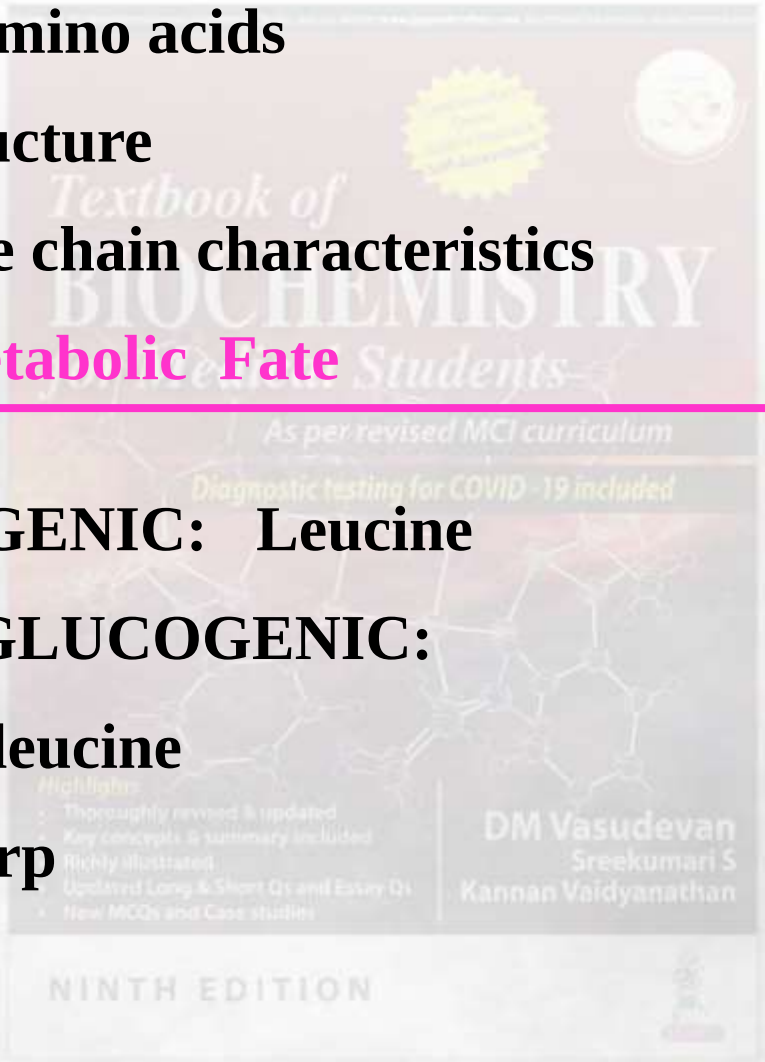
PURELY KETOGENIC: Leucine

KETOGENIC + GLUCOGENIC:

Lysine, Isoleucine

Phe, Tyr, Trp

GLUCOGENIC



I. Classification based on Structure

II. based on Side chain characteristics

III. Based on Metabolic Fate

IV. BASED ON NUTRITIONAL REQUIREMENT

- **ESSENTIAL / INDISPENSABLE**
  = 8 amino acids
  They cannot be synthesised in body
  So, if they are not available in the food growth cannot take place

- **PARTIALLY ESSENTIAL**
  = Arg, His, 2 amino acids

- **NON-ESSENTIAL / DISPENSABLE**

Partially essential

A arginine

H histidine

Essential

I isoleucine

L leucine

T threonine

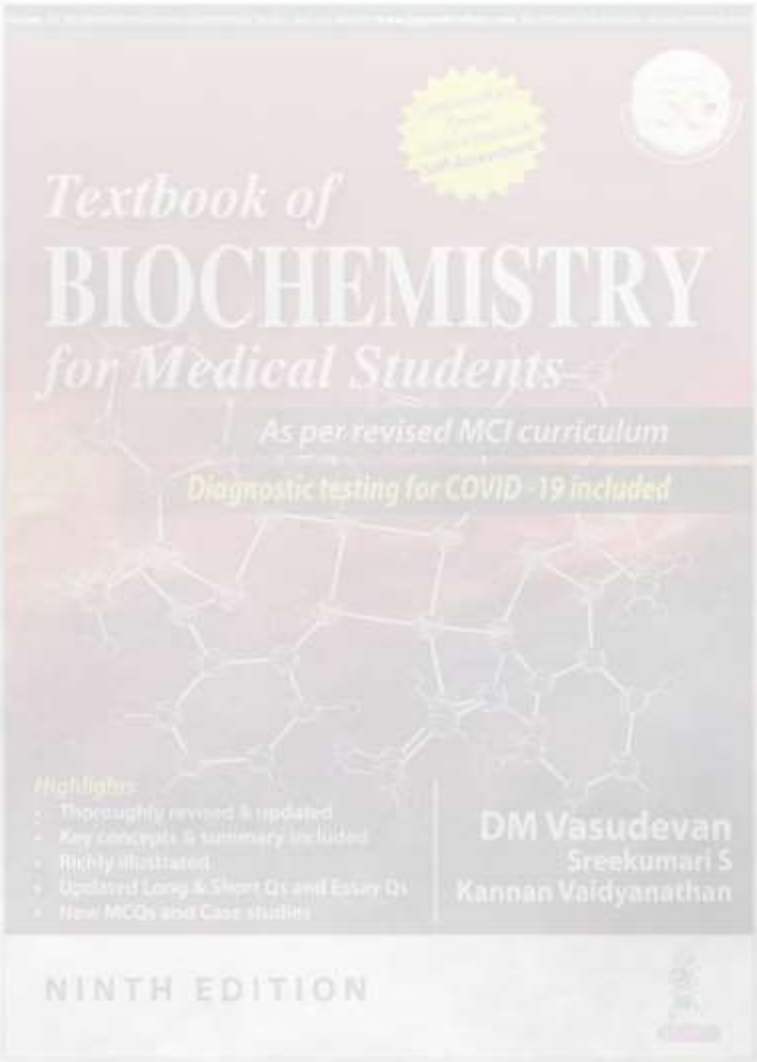
K lysine

M methionine

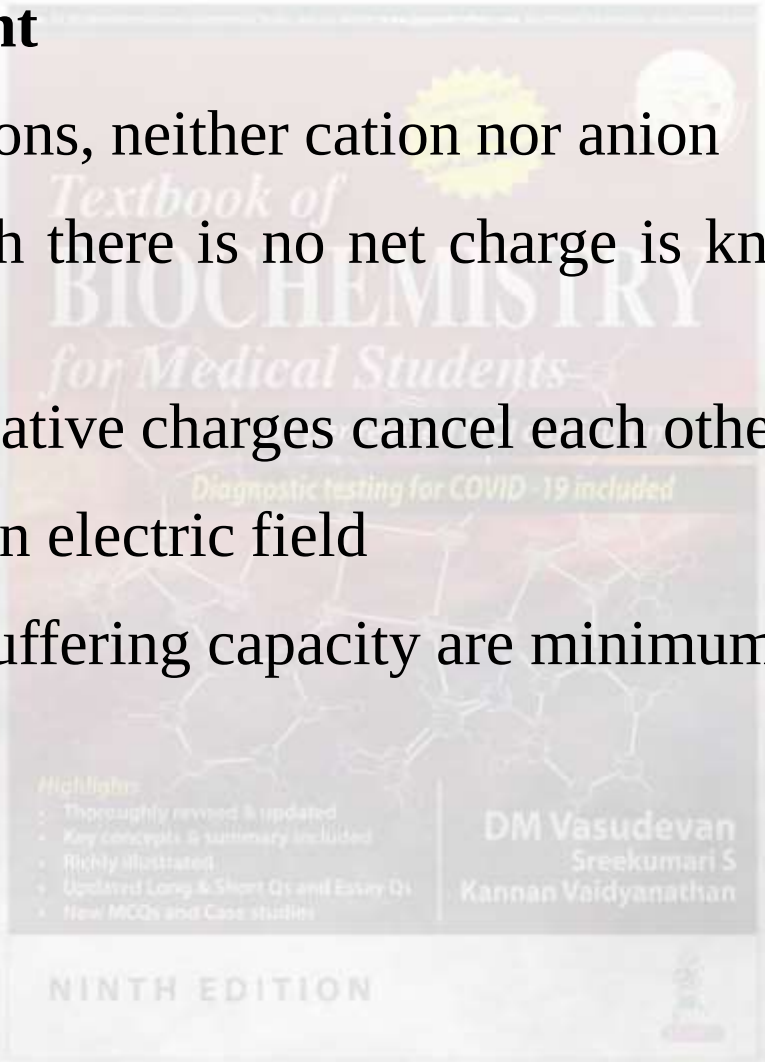
F phenylalanine

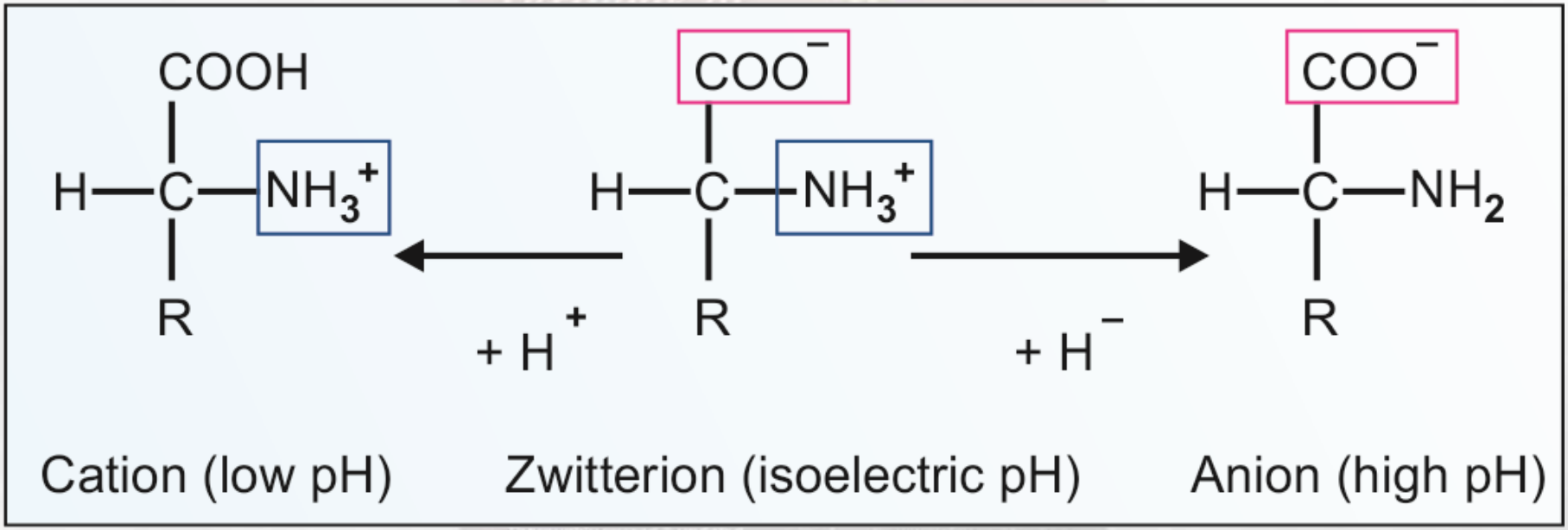
W tryptophan

V valine



- **Iso-electric point**
- Exist as zwitterions, neither cation nor anion
- The pH at which there is no net charge is known as iso-electric pH (point)
- Positive and negative charges cancel each other
- No mobility in an electric field
- Solubility and buffering capacity are minimum




COOH
H—C—NH3+
R
+ H+
COO−
H—C—NH3+
R
+ H−
COO−
H—C—NH2
R
Cation (low pH)
Zwitterion (isoelectric pH)
Anion (high pH)

ISO-ELECTRIC POINT

ISO-ELECTRIC pH (pI)

NO NET CHARGE

NO MOBILITY IN ELECTRIC FIELD

SOLUBILITY MINIMUM

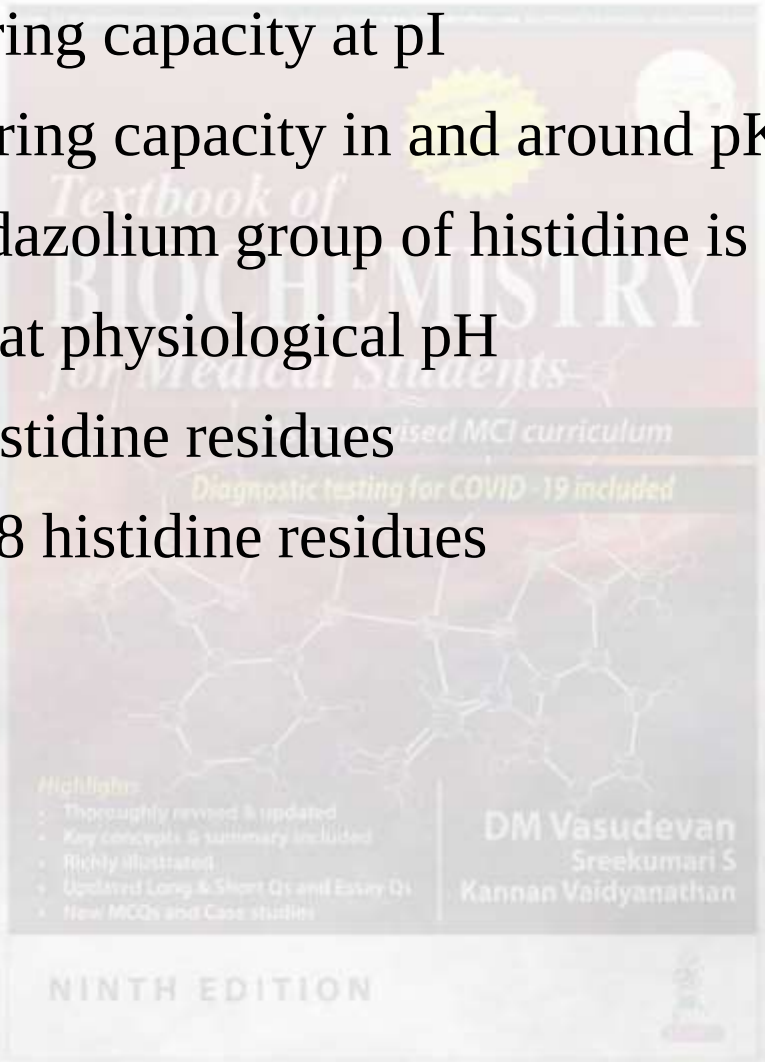
PRECIPITATION MAXIMUM

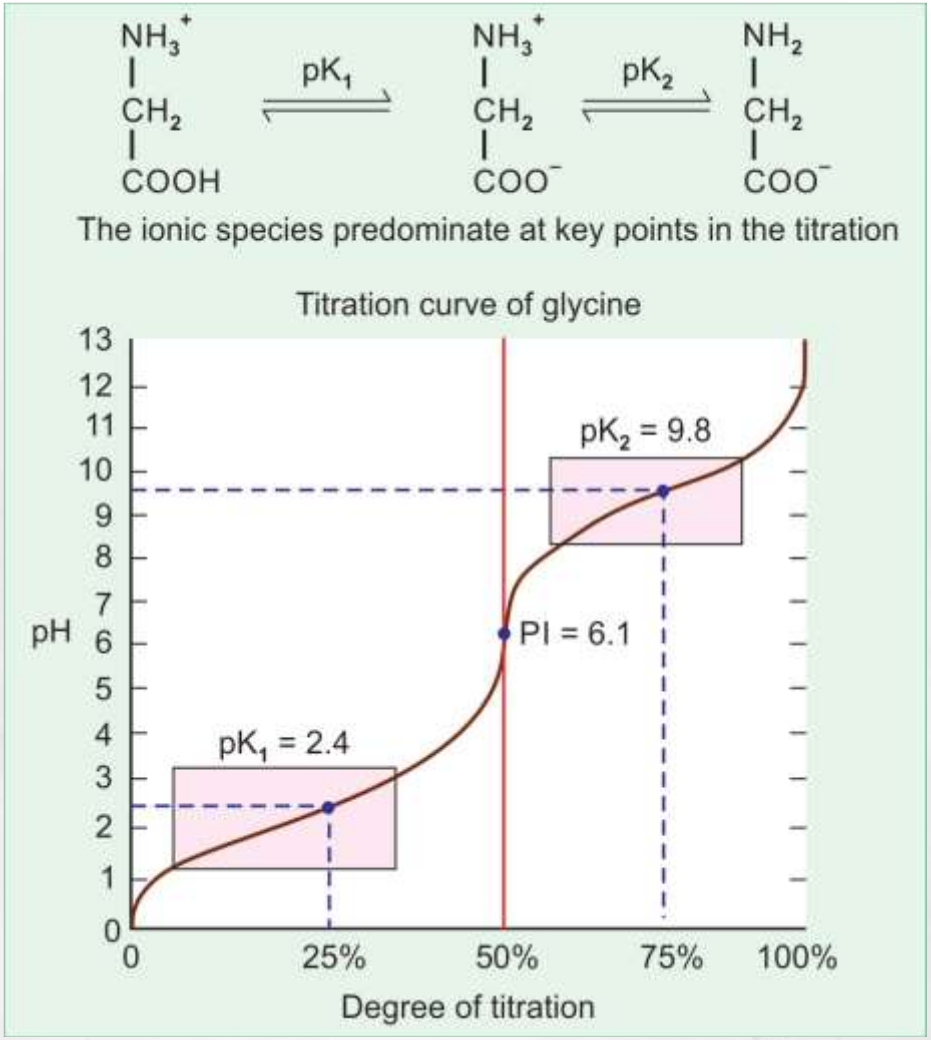
- **BUFFERING CAPACITY**
- **MINIMUM at pI**
- **MAXIMUM at pK1 and pK2**

pK of imidazole (histidine) = 6.1

Buffering Action of Amino Acids and Proteins

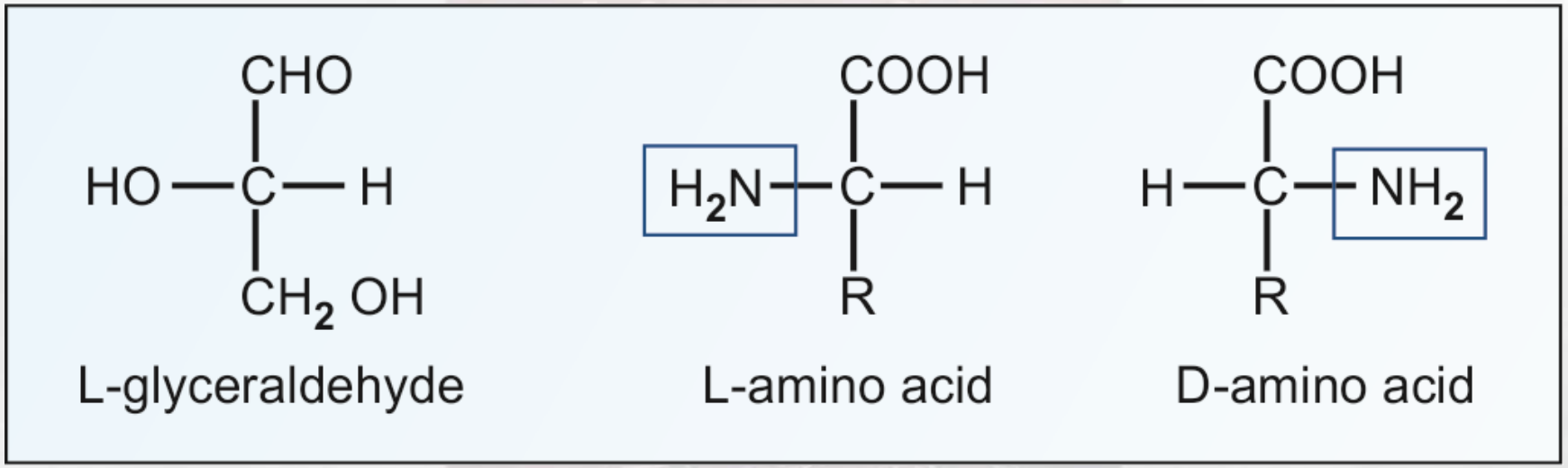
- Minimum buffering capacity at pI
- Maximum buffering capacity in and around pK_1 and pK_2
- pK value of imidazolium group of histidine is 6.1
- Effective buffer at physiological pH
- Albumin – 16 histidine residues
- Hemoglobin – 38 histidine residues





Titration curve of glycine

Optical Activity



Asymmetric Carbon atom

Optical Activity

GLYCINE - no optically active centre

ISOLEUCINE, THREONINE - 2 centres

4 diasterio isomers

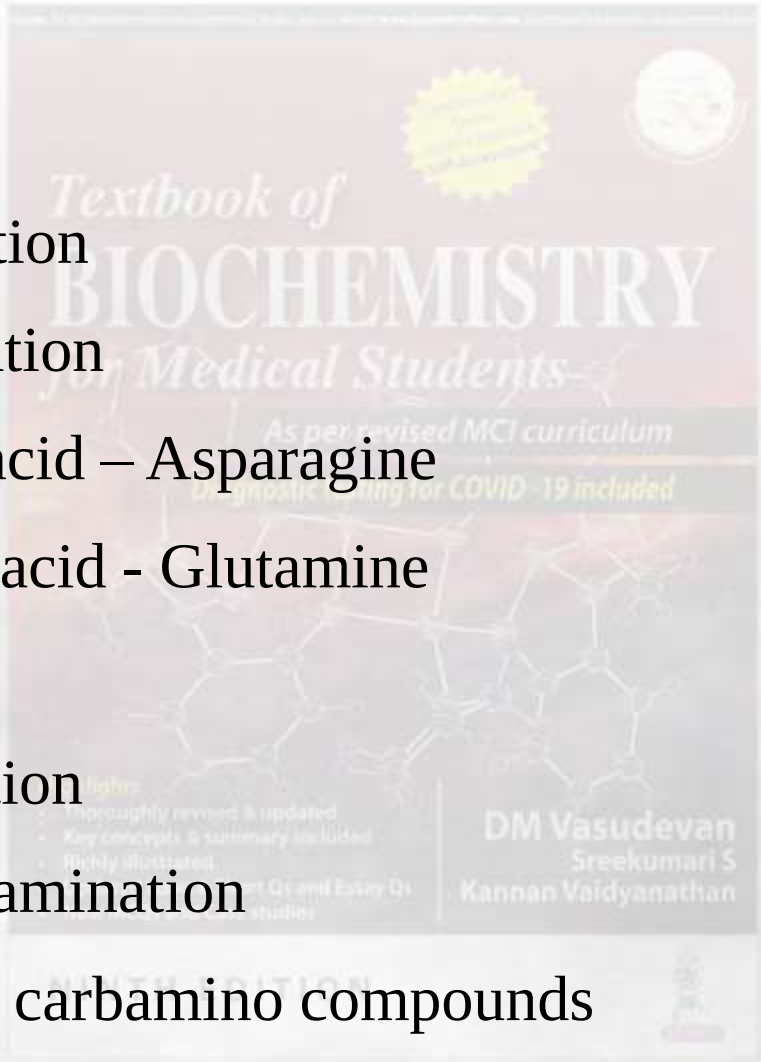
D VARIETY - Gramicidine, Polymyxin,

Actinomycin, Valinomycin

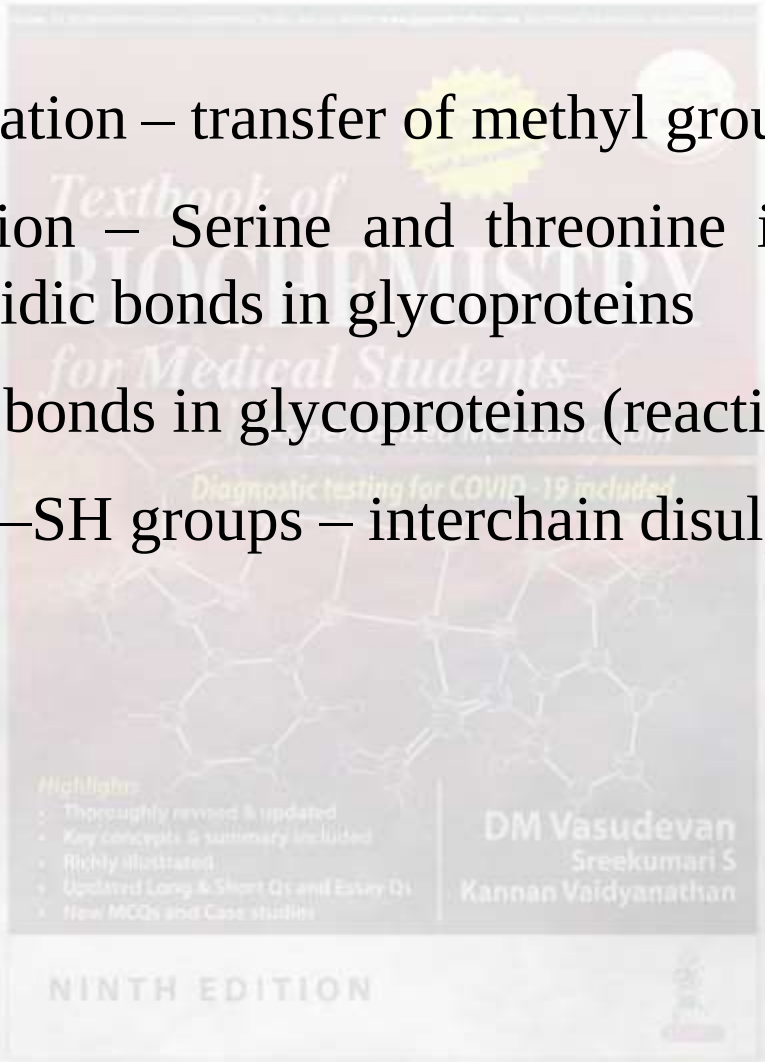
Bacterial peptidoglycans

Reactions of Amino Acids

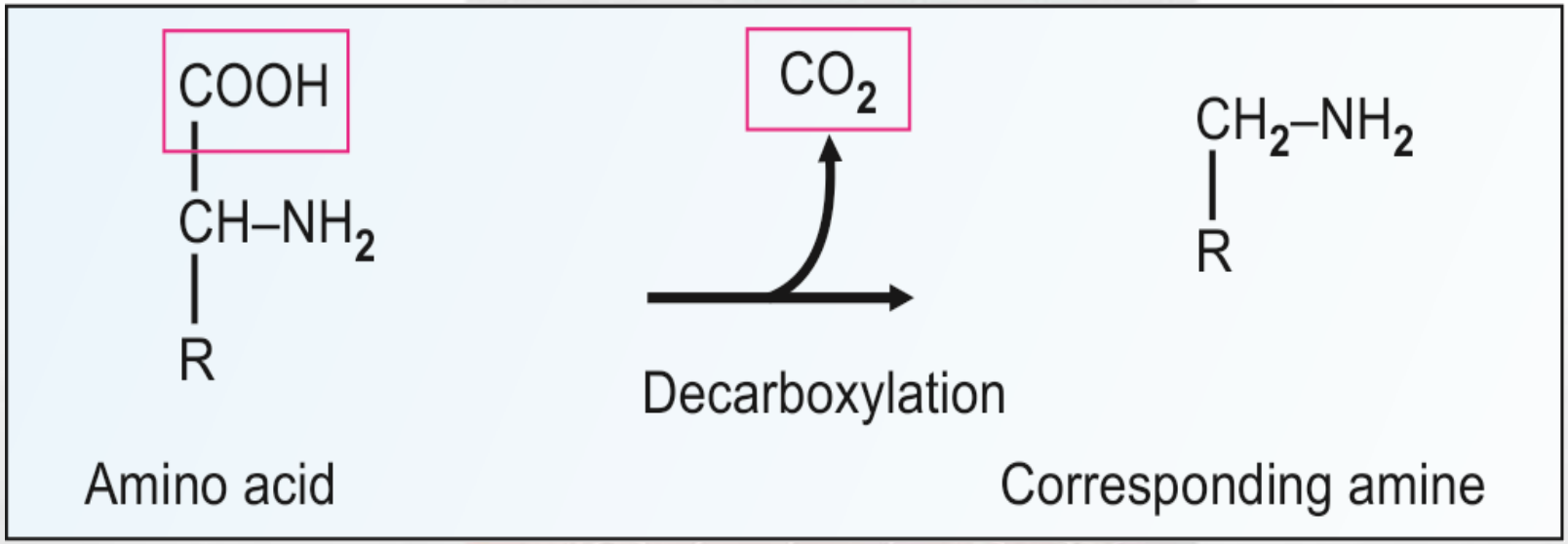
- Can be due to –
- Carboxyl group
  - Decarboxylation
  - Amide formation
    - Aspartic acid – Asparagine
    - Glutamic acid - Glutamine
- Amino group
  - Trans-amination
  - Oxidative deamination
  - Formation of carbamino compounds



- Side chains
  - Trans methylation – transfer of methyl group
  - Ester formation – Serine and threonine in phosphoproteins and O glycosidic bonds in glycoproteins
  - N glycosidic bonds in glycoproteins (reaction of amide group)
  - Reactions of –SH groups – interchain disulphide bonds



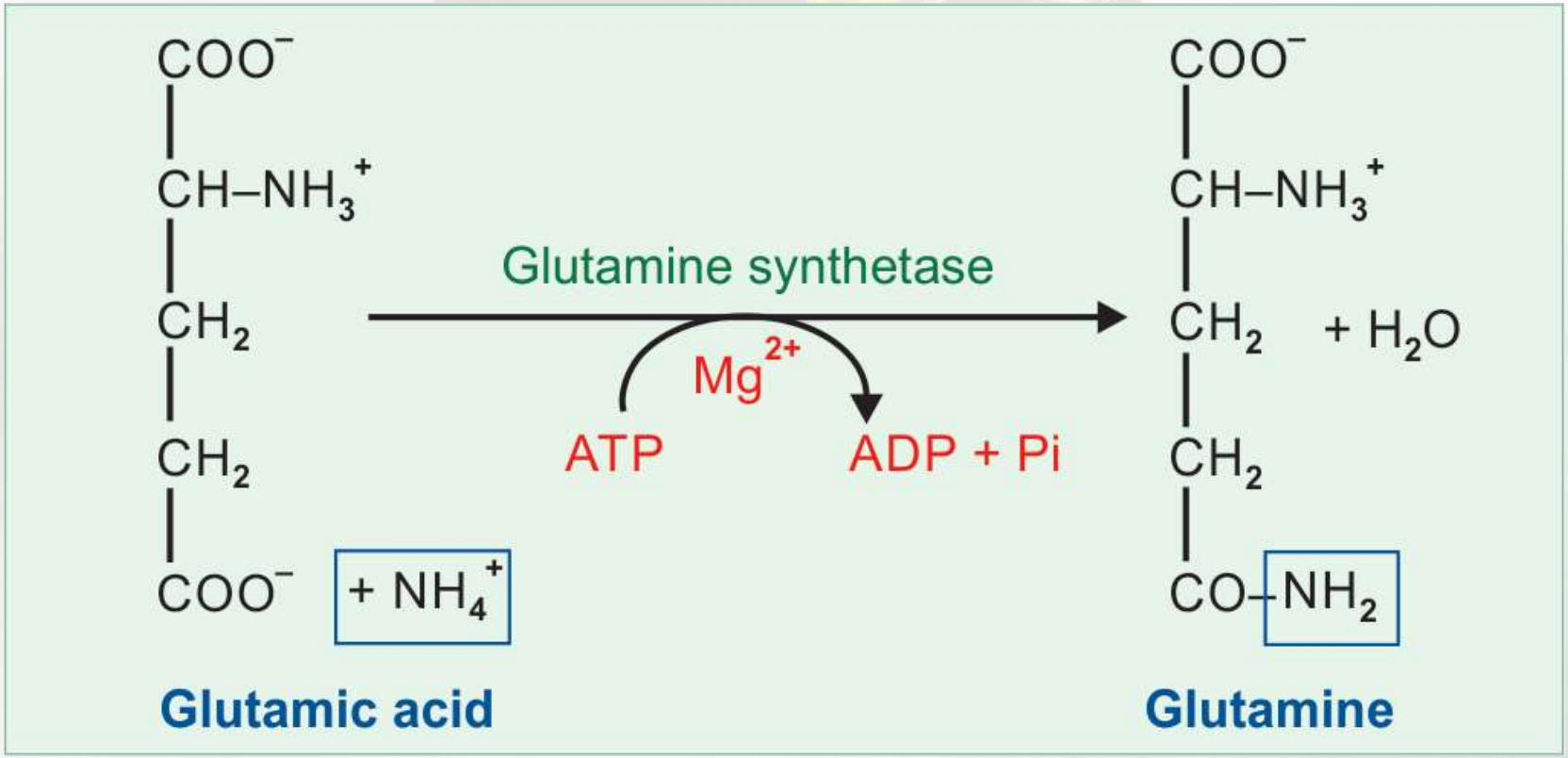
Decarboxylation



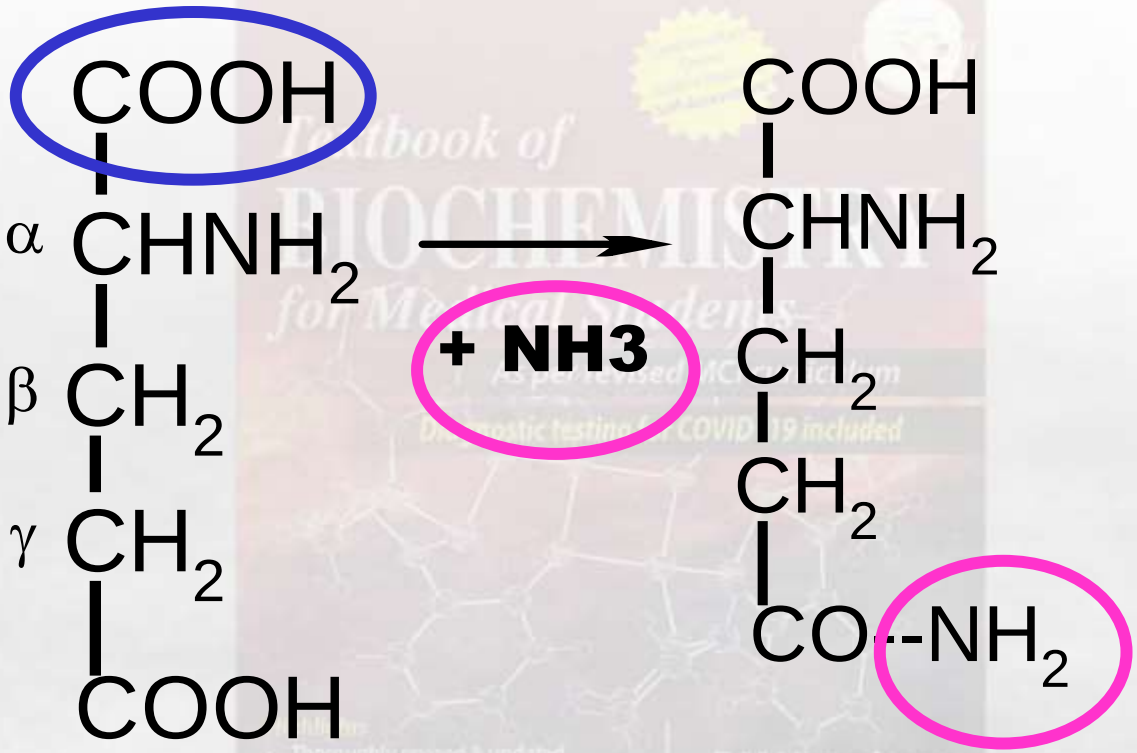
Histidine --> Histamine
Tryptophan --> Tryptamine
Tyrosine --> Tyramine

Glutamic acid --> GABA (gamma amino butyric acid)

Formation of Glutamine.



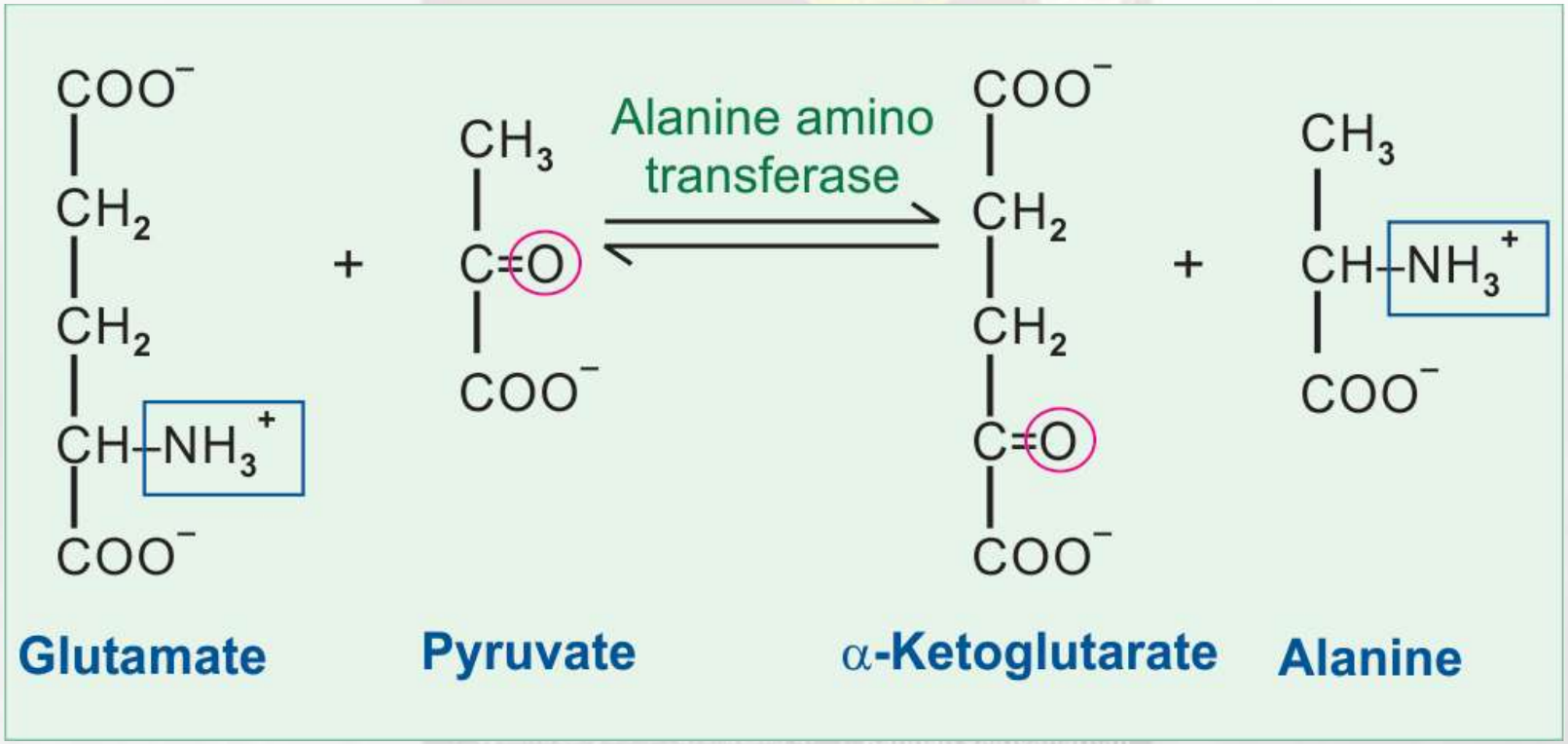
AMIDE FORMATION



Glutamic acid **Glutamine**

Aspartic acid **Asparagine**

Transamination



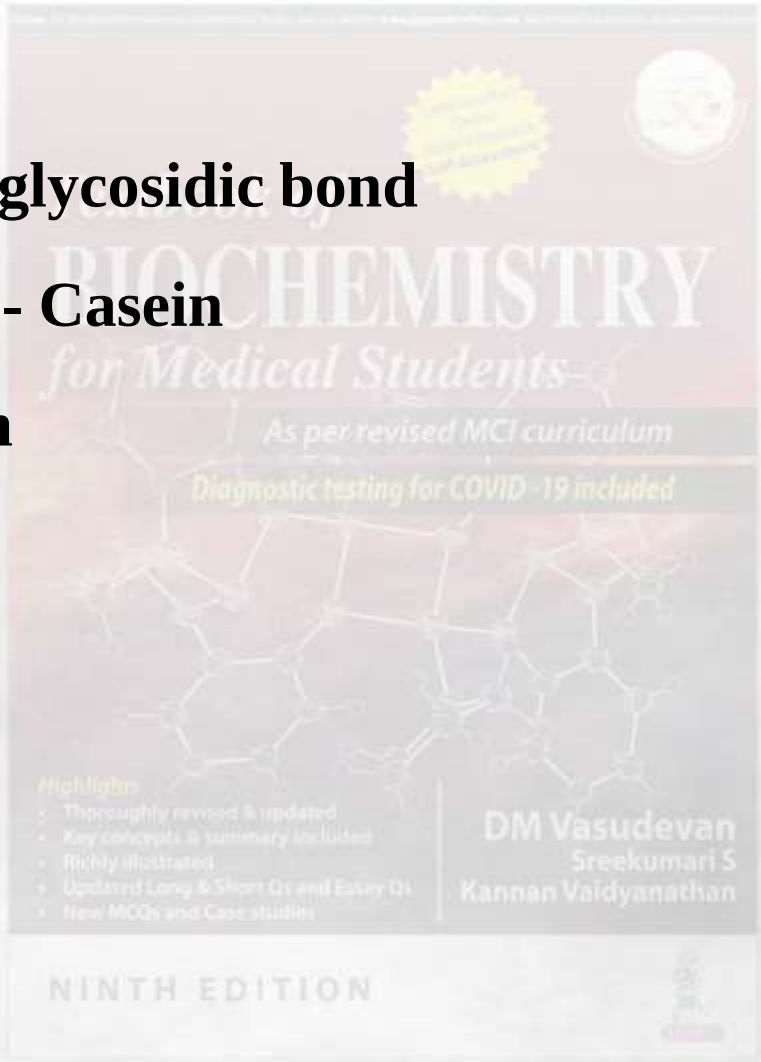
Hydroxyl Group

Serine Threonine

Glycoproteins; O-glycosidic bond

Phosphoproteins -- Casein

Enzyme activation



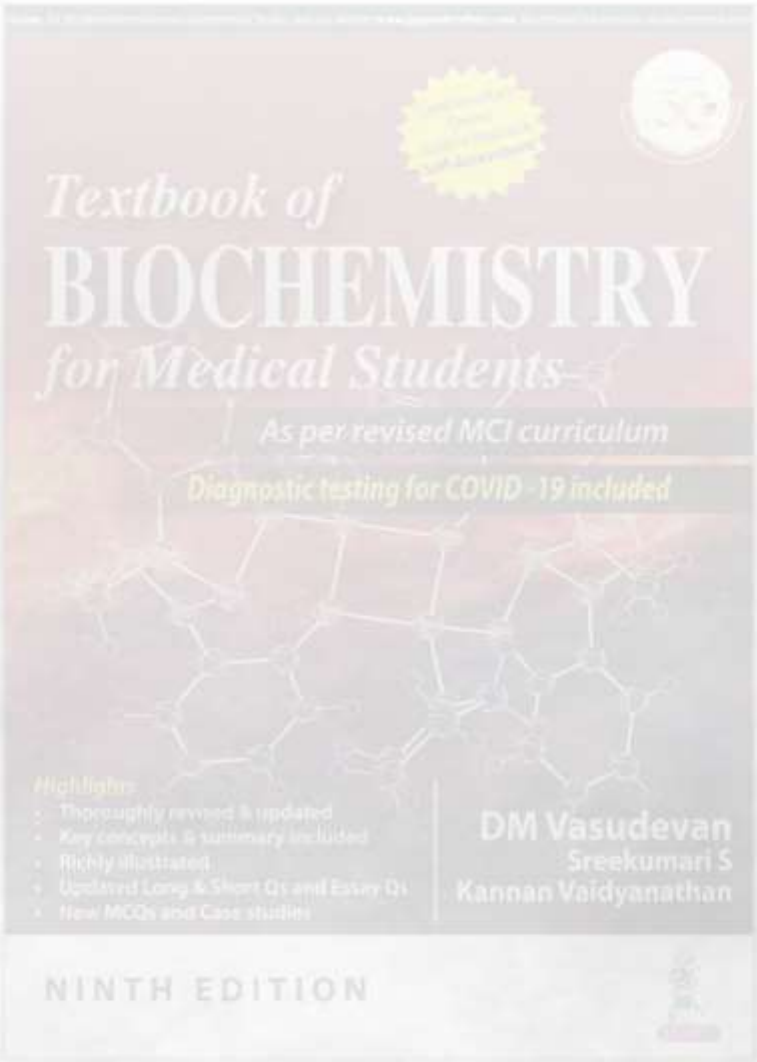
Amide Group

Asparagine

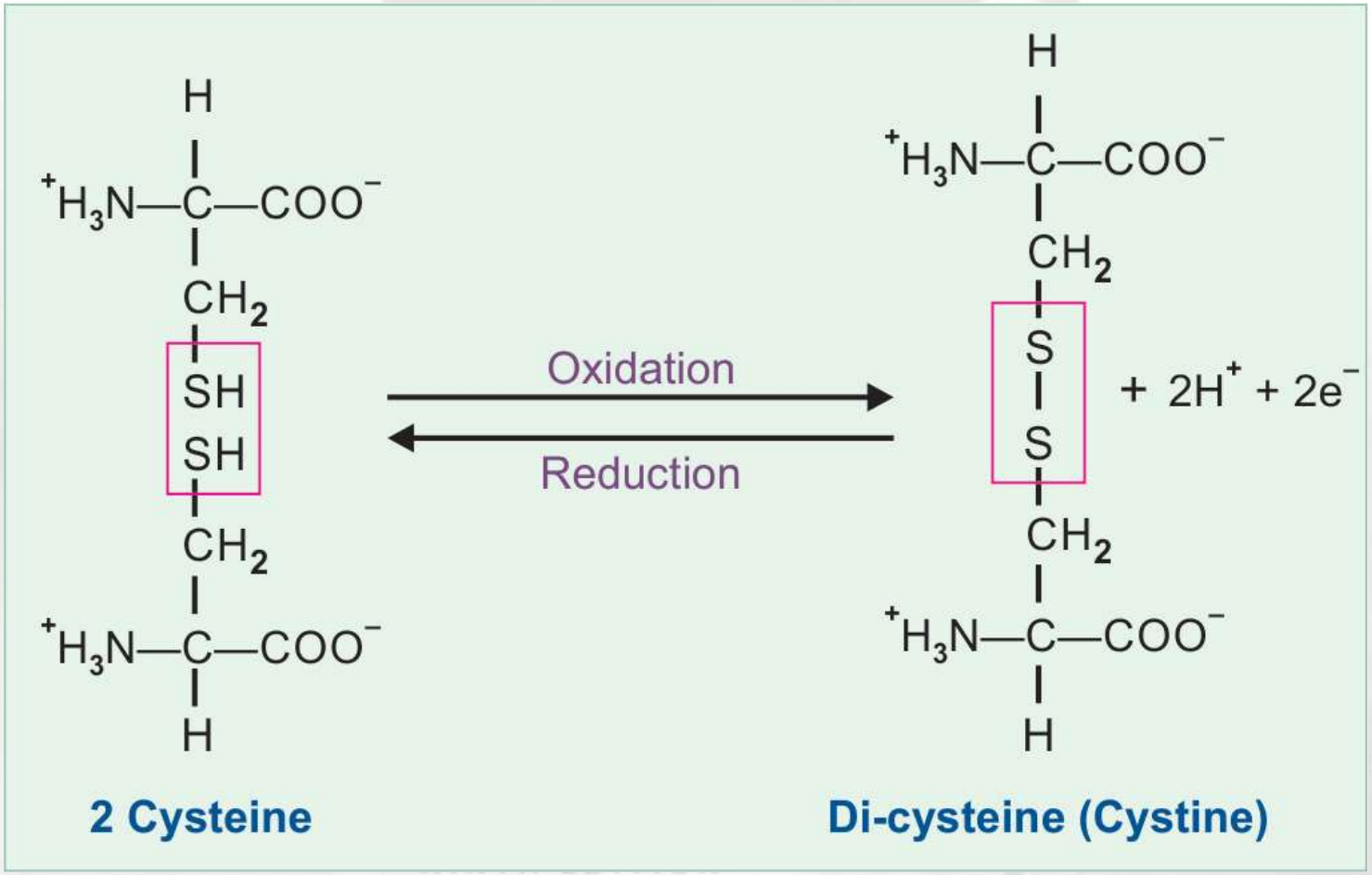
Glutamine

Glycoproteins

N-glycosidic bond



Disulphide Bridge (Linkage)



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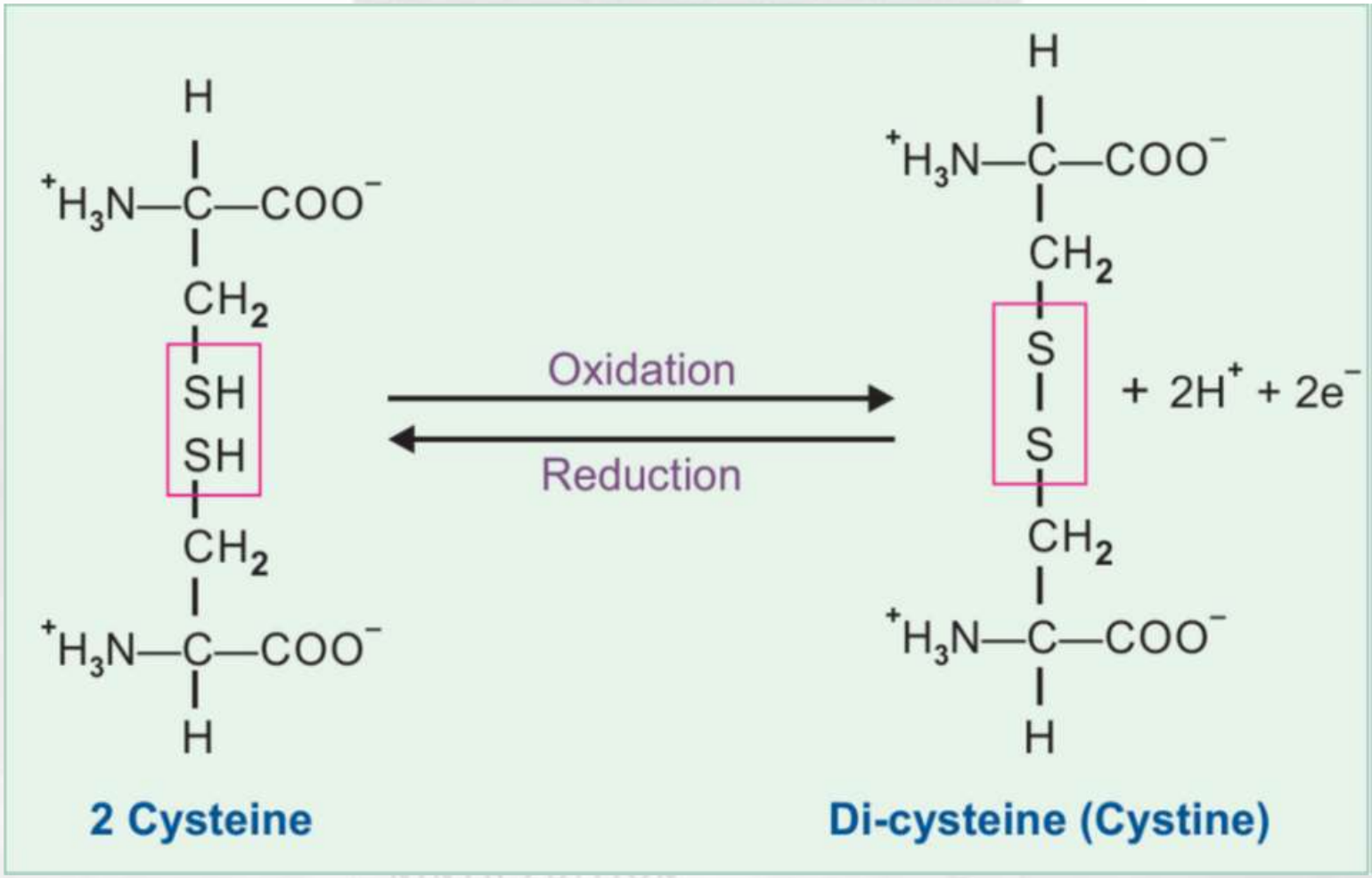
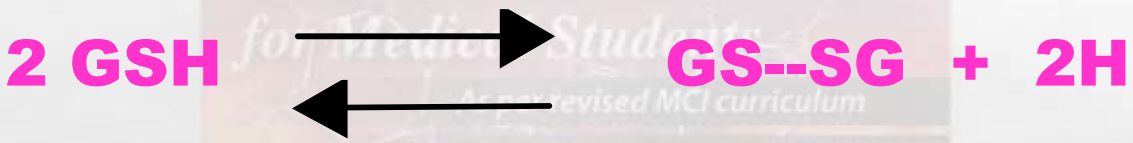


Glutathione

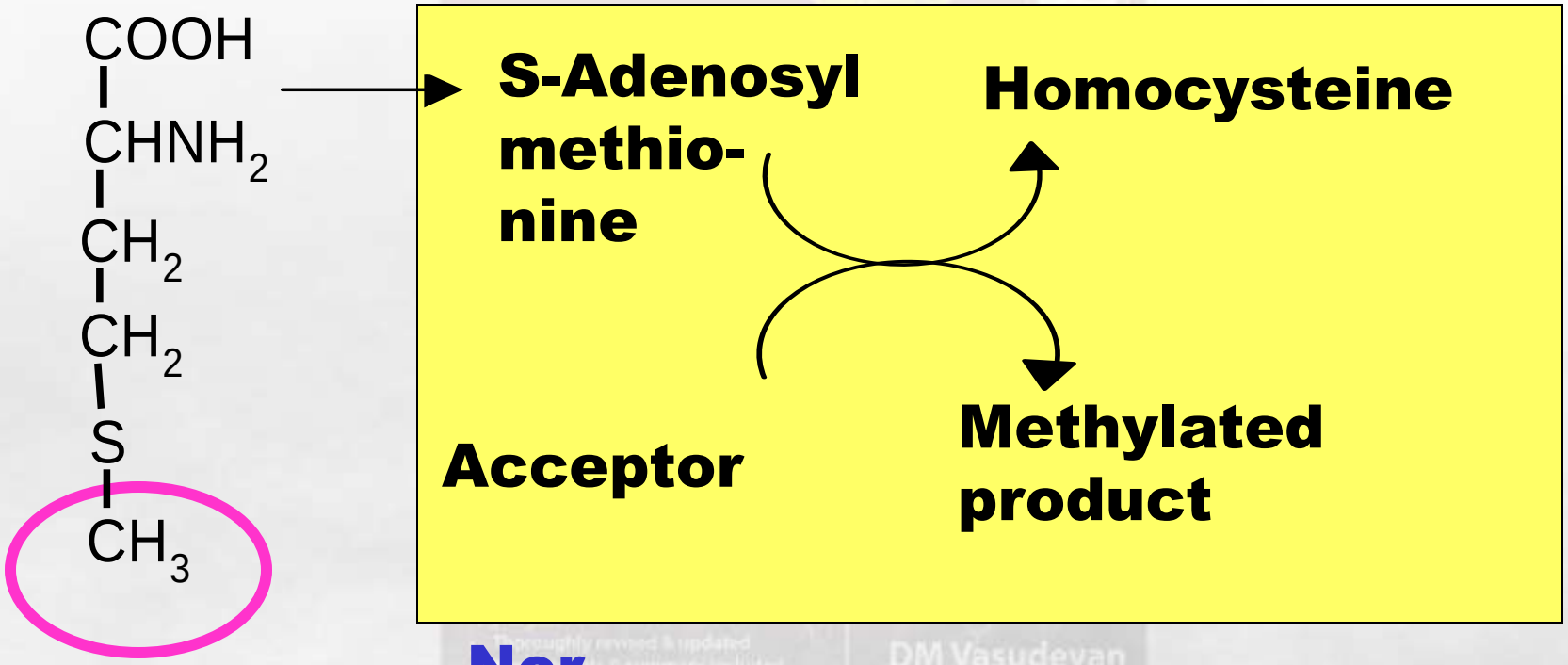
Glutamic acid + Cysteine + Glycine

Gamma Glytamyl Cysteinyl Glycine



Hydrogen acceptance / release
Activation of enzymes

Trans Methylation Methyl Transfer Reactions



Special Functions of Amino Acids

A. **Gamma amino butyric acid** (GABA, a derivative of glutamic acid) and dopamine (derived from tyrosine) are neurotransmitters.

B. **Histamine** (synthesised from histidine) is the mediator of allergic reactions.

C. **Thyroxine** (from tyrosine) is an important thyroid hormone.

D. **Serine** forms the active centre of many proteolytic enzymes.

E. **Histidine** residues are important in the buffering activity of proteins.

F. **Lysine** group is involved in the binding of co-enzymes pyridoxal phosphate and biotin.

G. **Ornithine** and citrulline are derivatives of arginine, and are essential for urea synthesis.

Color Reactions of Amino Acids

- Ninhydrin test – Alpha amino group
- Biuret reaction – Peptide group
- Xanthoproteic test – Benzene ring (Phe, Tyr, Trp)
- Millon's test – Phenol ring (Tyr)
- Aldehyde test – Indole ring (Trp)
- Sakaguchi test – Guanidium group (Arg)
- Sulphur test – SH group (Cysteine)
- Nitroprusside test – SH group (Cysteine)
- Pauly's test – Imidazile group (His)

Importance of side chains of amino acids:

α carboxy groups and a amino groups in proteins are unavailable as they form peptide bonds; nature of side chains determine physical properties, including protein folding.

Non-polar side chain	Uncharged polar side chains	Acidic side chains	Basic side chains
Alanine	Asparagine	Aspartic acid	Arginine
Glycine	Cysteine	Glutamic acid	Histidine
Isoleucine	Glutamine		Lysine
Leucine	Serine		
Methionine	Threonine		
Phenylalanine	Tyrosine		
Proline			
Tryptophan			
Valine			

Found on the outside of proteins that function in an aqueous environment and in the interior of membrane-associated proteins

Found in the interior of proteins that function in an aqueous environment and on the surface of proteins (such as membrane proteins) that interact with lipids