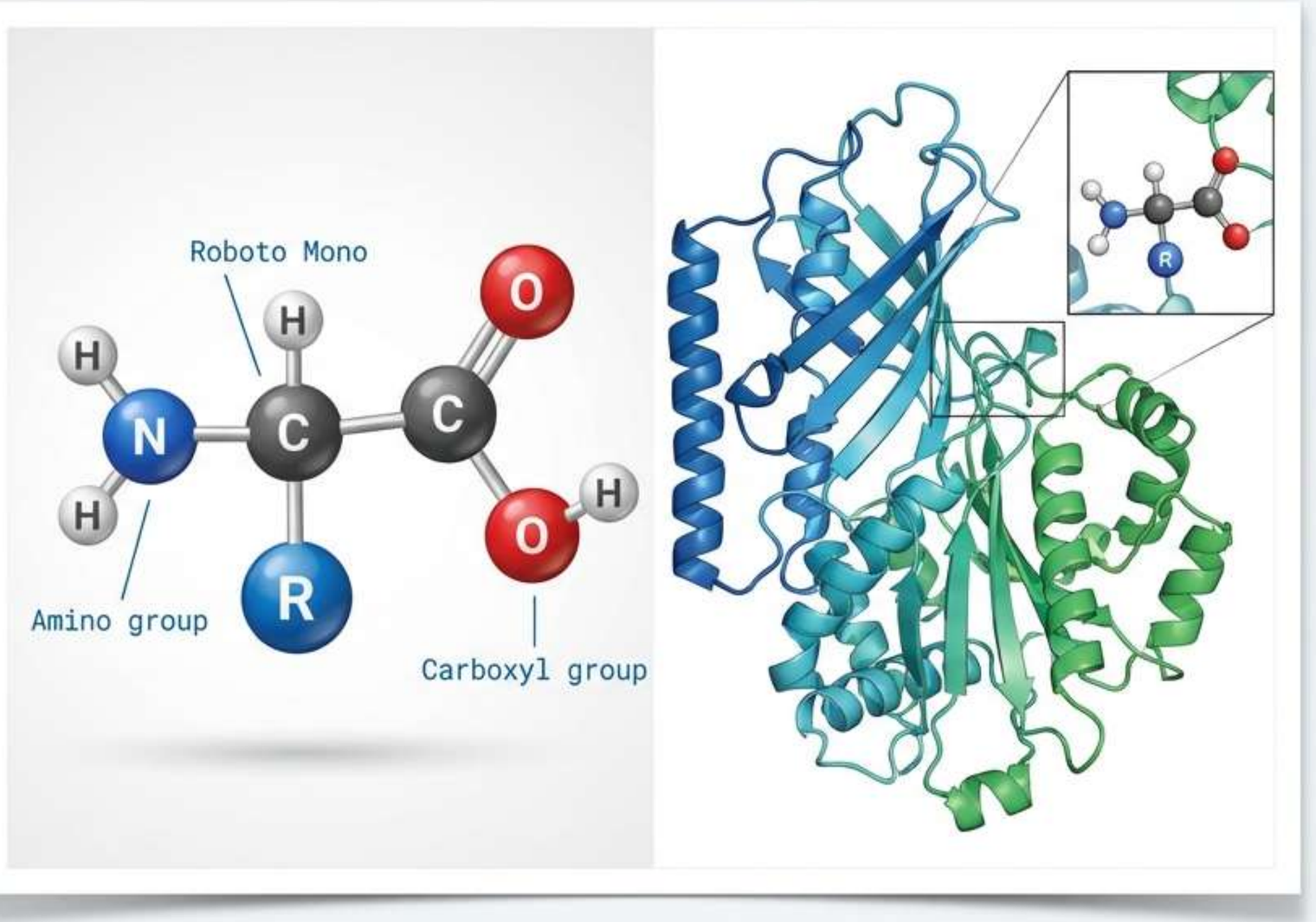
From Building Blocks to Biological Machines

Amino Acids & Proteins: A Comprehensive Study Guide for Dental Medicine

Core Definition: Amino acids are the structural units (monomers) of proteins, constituting >50% of the dry weight of cells.

The Narrative Arc:

1. **The Bricks:** Structure & Classification
2. **The Mortar:** Physical & Chemical Properties (pHi)
3. **The Architecture:** Protein Structure (1^0 to 4^0)
4. **The Toolbox:** Purification & Analysis
5. **Exam Strategy:** Analysis of Past Questions & Traps



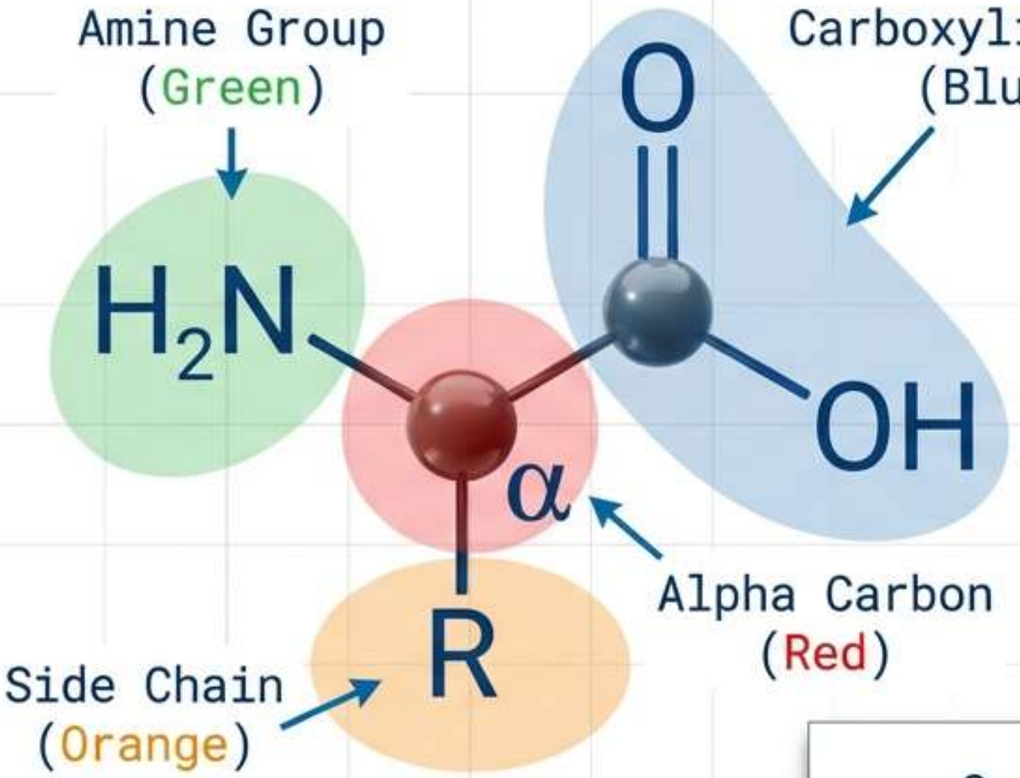
The Fundamental Structure: The Central Dogma

in Helvetica Now Display Bold in Scientific Blue

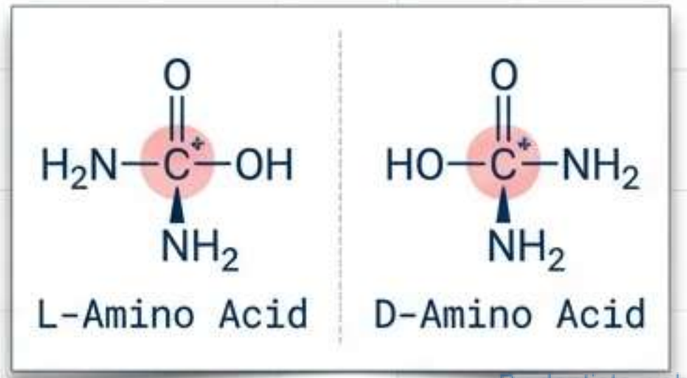
Common Structure: All AAs possess a carboxylic acid (-COOH) and a primary amine (-NH2) on the same alpha-carbon (*Cα*).

Stereoisomerism:

- All AAs (Except **Glycine**) have an asymmetric carbon (*C**) and are **Chiral**.
- **Enantiomers**: D- and L-series. Natural proteins primarily use **L-amino acids**.



REF Q1: Glycine is the ONLY achiral amino acid (R = H). It has no asymmetric carbon.



Classification I: Polarity Overview

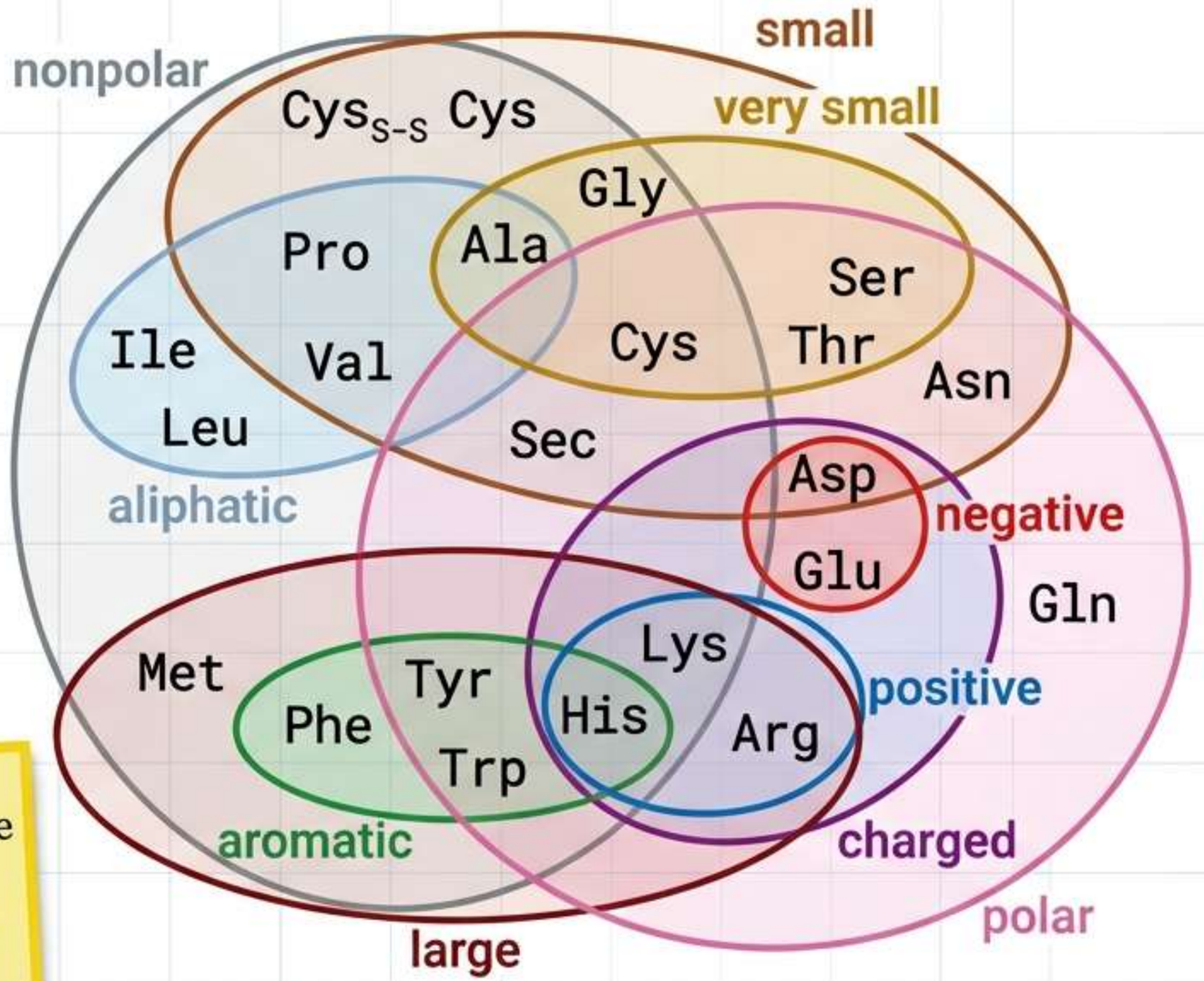
1. Non-Polar (Hydrophobic):

- Found in the *interior* of proteins (Hydrophobic Effect).
- Aliphatic: Gly, Ala, Val, Leu, Ile, Pro.
- Aromatic: Phe, Trp.
- Sulfur: Met.

2. Polar (Hydrophilic):

- **Uncharged:** Ser, Thr, Cysteine, Asn, Gln, Tyr.
- **Charged:** Asp, Glu (Negative) / Lys, Arg, His (Positive).

REF Q6: Leucine is Aliphatic, Branched, and Hydrophobic.



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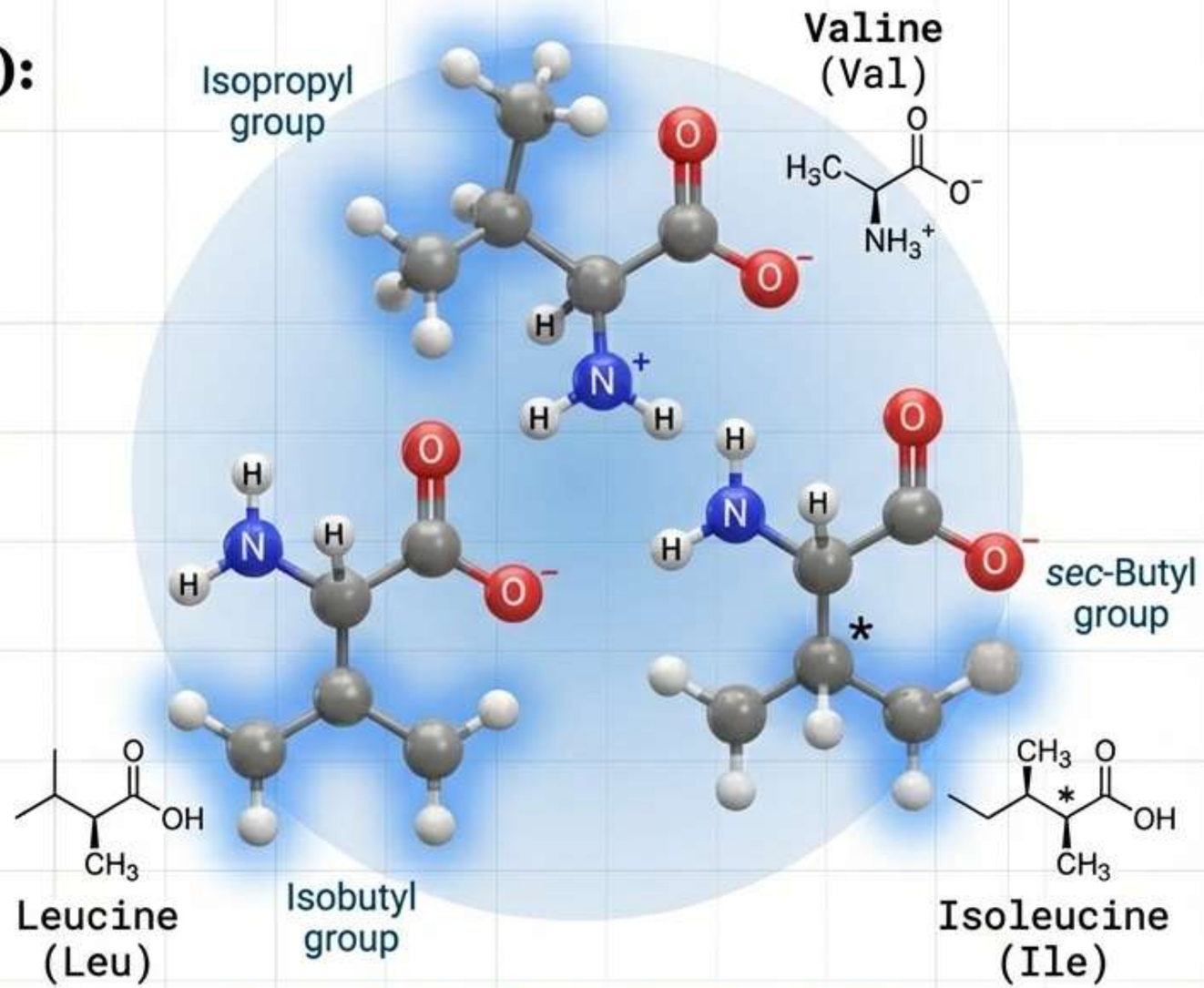
Classification II: Aliphatic & Branched Chain (BCAA)

Branched-Chain Amino Acids (BCAA):

- **Valine (Val, V):** Isopropyl group. Essential.
- **Leucine (Leu, L):** Isobutyl group. Essential & Strictly Ketogenic.
- **Isoleucine (Ile, I):** *sec*-Butyl group. Essential, Glucogenic & Ketogenic.

REF Q23: Valine is essential and non-polar.

REF Q3: Isoleucine (and Threonine) has TWO asymmetric carbons.

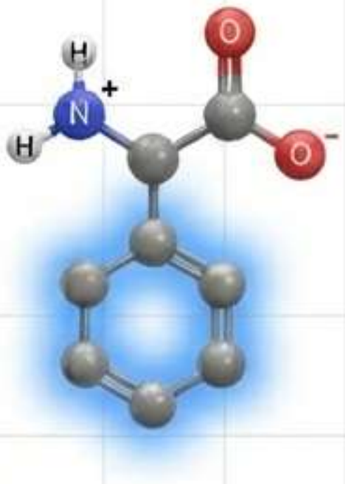


Branched-Chain Amino Acids

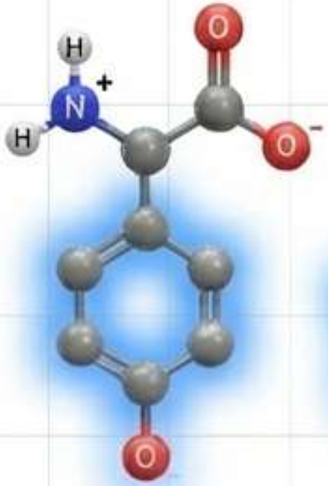
Classification III: Aromatic & Cyclic Side Chains

Aromatic Amino Acids:

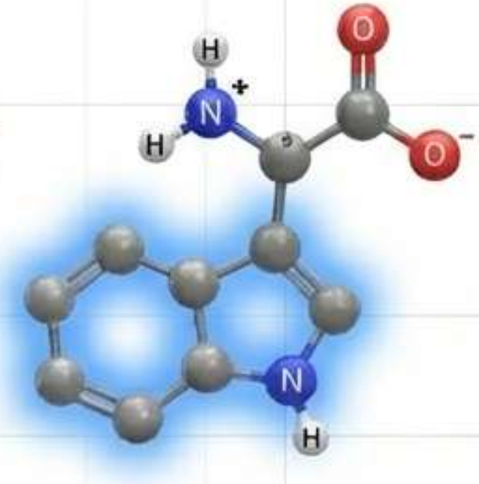
- **Phenylalanine (Phe, F):** Benzene ring. Hydrophobic.
- **Tyrosine (Tyr, Y):** Phenol group (-OH). Can be phosphorylated. Absorbance at 280nm.
- **Tryptophan (Trp, W):** Indole ring. Highest UV absorbance. Destroyed by acid hydrolysis [REF Q29].



Phenylalanine
(Phe, F)
F



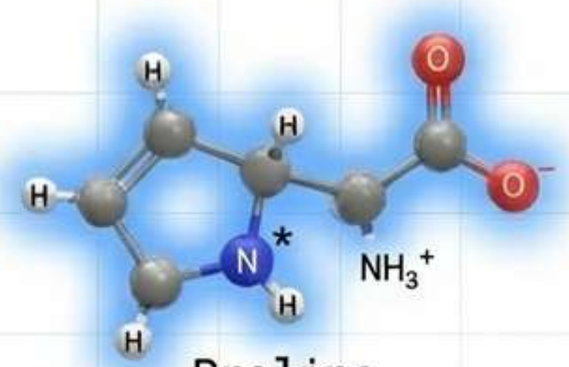
Tyrosine
(Tyr)
Y



Tryptophan
(Trp)
W

Special Case:

- **Proline (Pro, P):** Cyclic imino acid (secondary amine). Rigid structure disrupts α-helices.



Proline

Exam Note:
REF Q16-2: Phenylalanine single letter code is F.

Classification IV: Sulfur & Hydroxyl Groups

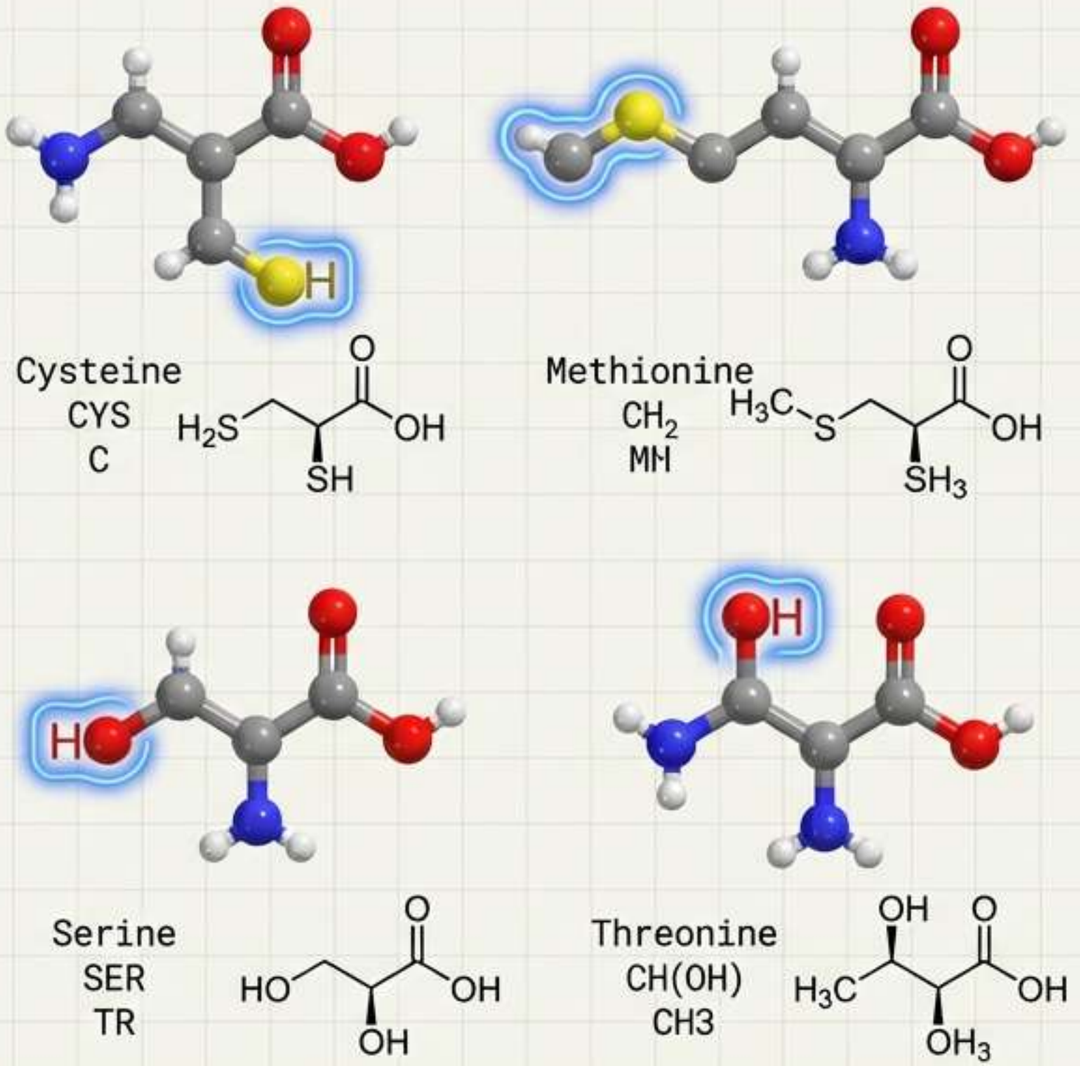
Sulfur-Containing:

- **Cysteine (Cys, C):** Thiol (-SH). Forms covalent **Disulfide Bridges**.
- **Methionine (Met, M):** Thioether. Start codon (AUG). Cleaved by BrCN [REF Q42].

Hydroxyl-Containing (Alcohols):

- **Serine (Ser, S)** & **Threonine (Thr, T):** Polar uncharged.
- **Function**: Site of O-linked glycosylation and **Phosphorylation** (along with Tyr).

Exam Note:
REF Q5: Phosphorylation occurs on -OH groups (Ser, Thr, Tyr).



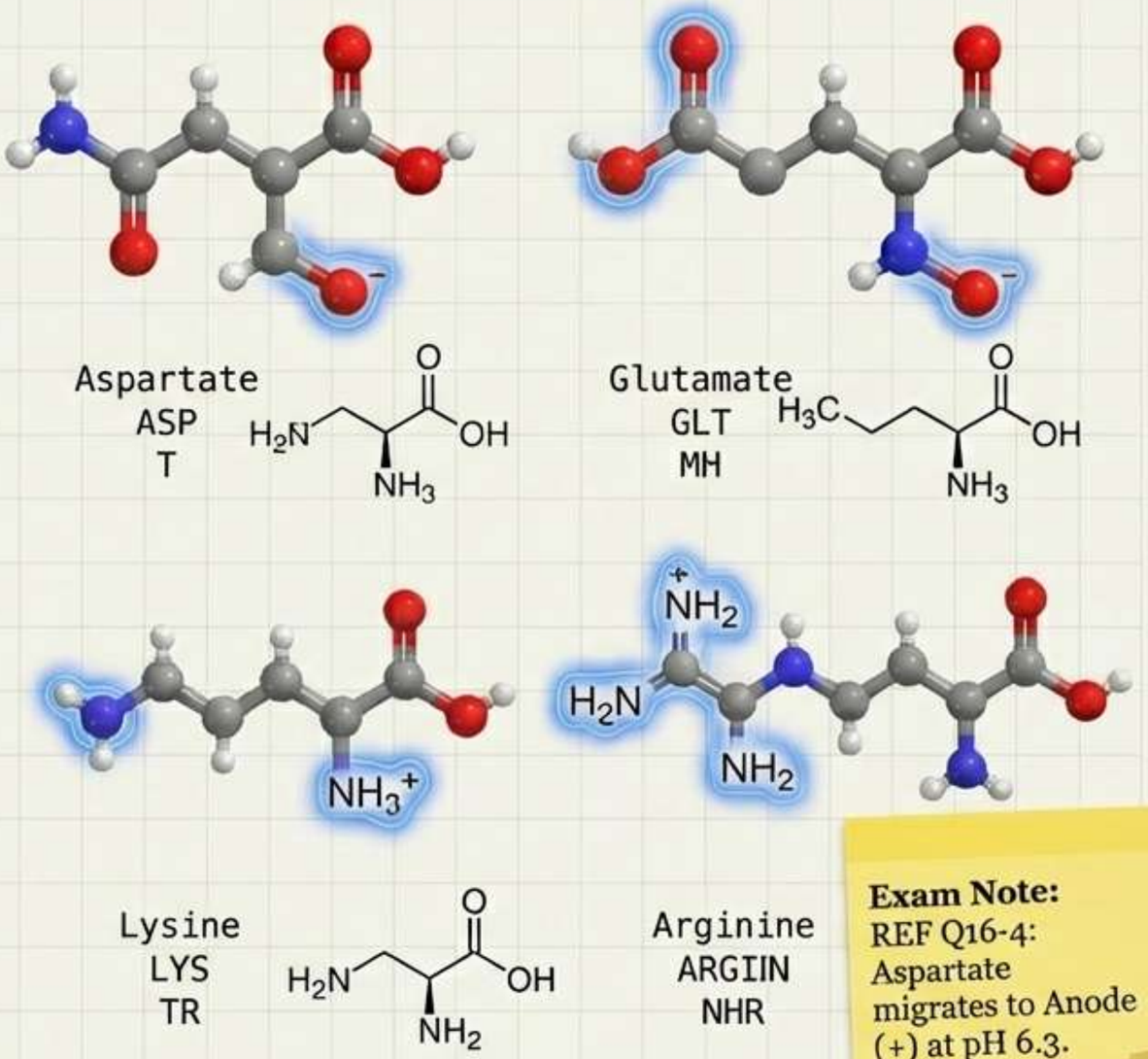
Classification V: The Charged Amino Acids

Acidic (Negatively Charged at pH 7):

- **Aspartate (Asp, D) & Glutamate (Glu, E):** Second carboxyl group.
- **Amide Derivatives:** Asparagine (**Asn**) and Glutamine (**Gln**).

Basic (Positively Charged at pH 7):

- **Lysine (Lys, K):** Primary amine at ε-carbon.
- **Arginine (Arg, R):** Guanidinium group. Very high pHi (~10.76).
- **Histidine (His, H):** Imidazole ring. Buffering capacity near neutral pH.



Exam Note:
REF Q16-4: Aspartate migrates to Anode (+) at pH 6.3.

Nutritional Classification: The Essentials

Essential Amino Acids: Cannot be synthesized de novo. Must be ingested.

The List (8): Leu, Thr, Lys, Trp, Phe, Val, Met, Ile.

Mnemonic (French):
« Le Très Lyrique Tristan Fait Vachement Méditer Iseult »
(Leu - Thr - Lys - Trp - Phe - Val - Met - Ile)

Semi-Essential: Arginine & Histidine (Growth/Infants).

Exam Note:
REF Q23: Valine is Essential.

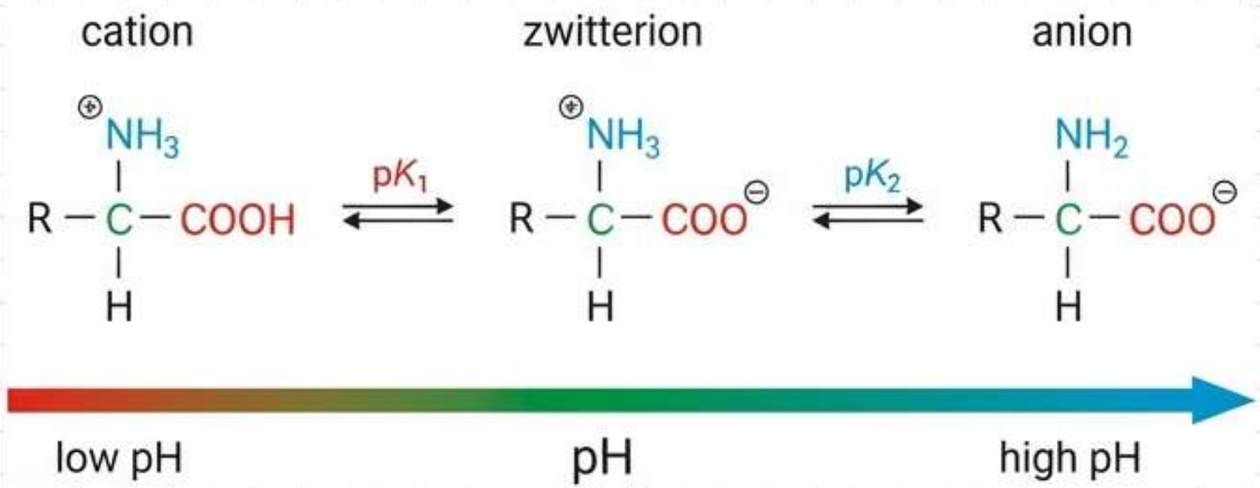
LEUCINE
Roboto Mono
THREONINE
LYSINE
Roboto Mono
Roboto Mono
TRYPTOPHAN
PHENYLALANINE
VALINE
Roboto Mono
METHIONINE
ISOLEUCINE

Physical Properties: Ionization & Zwitterions

Amphoteric Nature: Acts as both acid (proton donor) and base (proton acceptor).

The Zwitterion:

* At pH = pHi, the molecule is electrically neutral (Net charge = 0).
* Maximal number of charges, but net is zero.
* **Properties at pHi:** Minimal solubility (precipitation risk), No migration in electric field.



Exam Note: REF Q30: At pHi, the compound does not migrate.

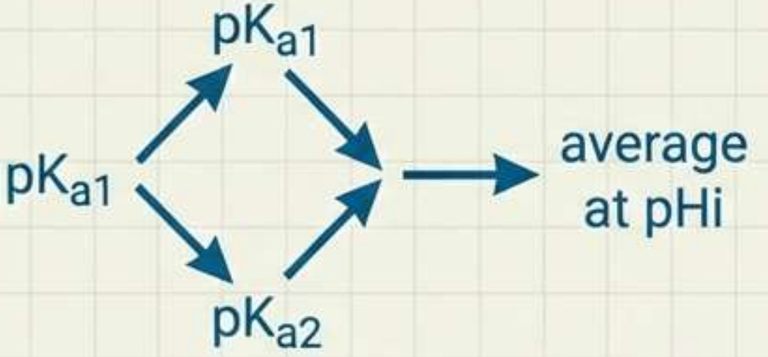
The Isoelectric Point (pHi): Calculations

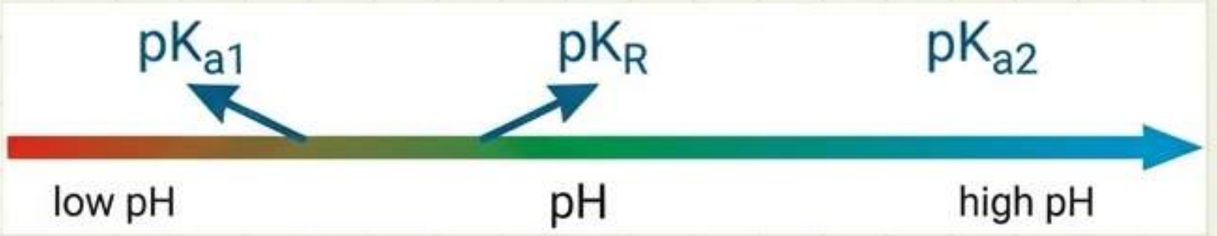
Definition: The pH at which net charge is zero.

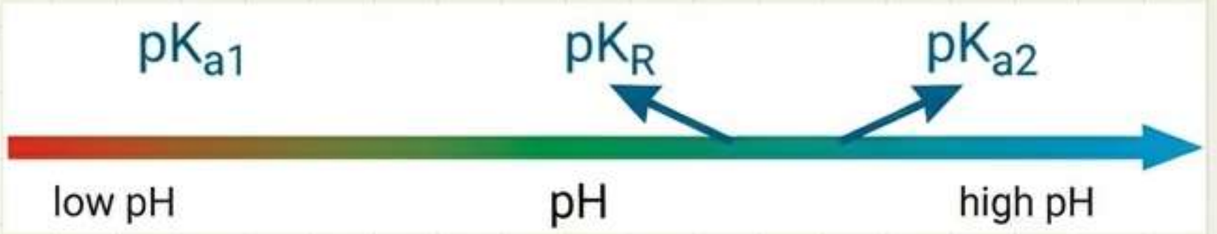
Calculation Rules:

1. **Neutral AA:** Average of pKa1 (COOH) and pKa2 (NH_3).
2. **Acidic AA (Asp, Glu):** Average of the two *lowest* pKas (COOH groups).
   $$pHi = (pKa\_1 + pK\_R) / 2$$
3. **Basic AA (Lys, Arg, His):** Average of the two *highest* pKas (Amino groups).
   $$pHi = (pK_R + pKa\_2) / 2$$

Exam Note:
REF Q24:
Glutamate
(2.1, 9.5, 4.1).
pHi = (2.1 + 4.1) / 2 = 3.1







Protein Structure: Primary & Secondary

Primary Structure:

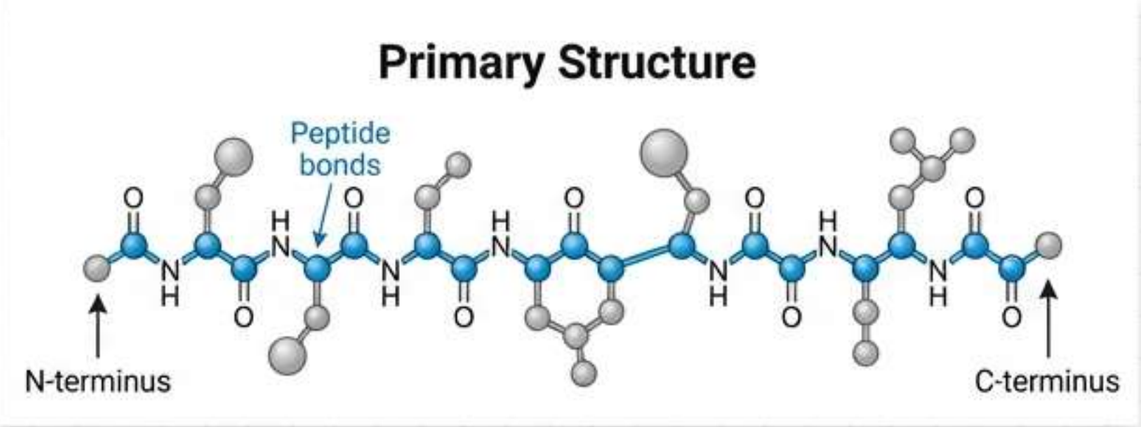
- Linear sequence of amino acids.
- Linkage: **Peptide Bond** (Covalent, Amide, Rigid/Planar).

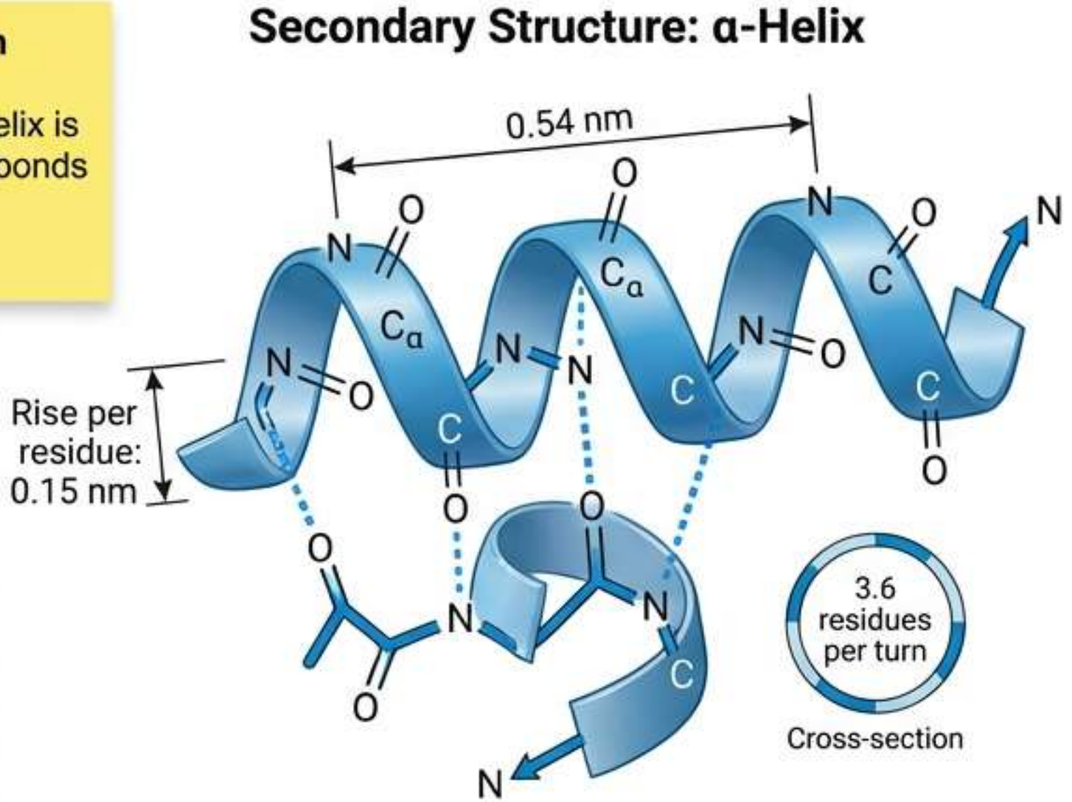
Secondary Structure:

- **α-Helix**: Right-handed spiral. 3.6 residues/turn. Stabilized by H-bonds (n to n+4) parallel to axis. [REF Q11]
- **β-Sheet**: Parallel or Anti-parallel strands. H-bonds perpendicular to axis.
- **β-Turns**: Reverses direction. Often contains Pro & Gy.

Exam Question

[REF Q11]: α-Helix is stabilized by H-bonds parallel to axis.





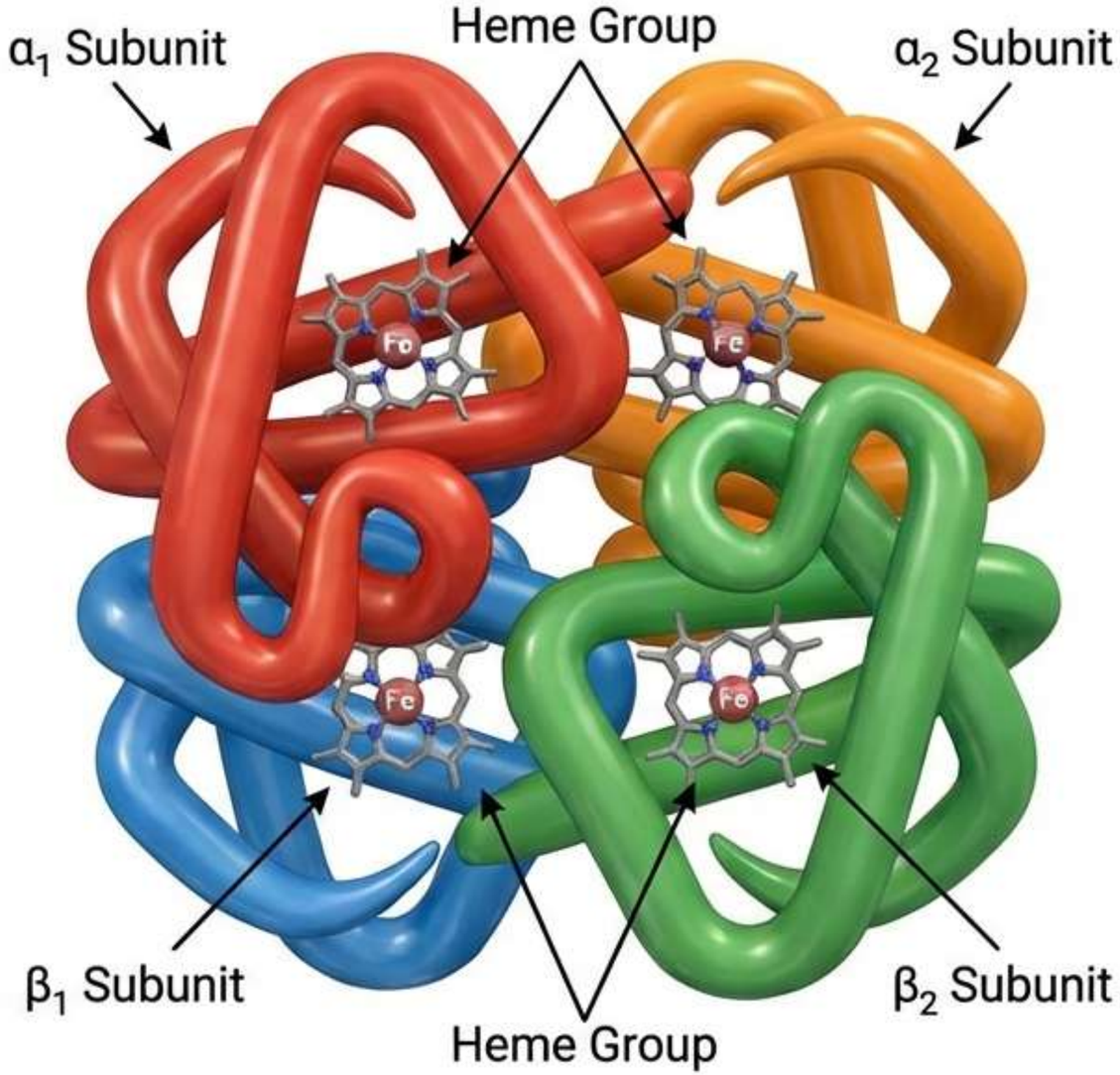
Tertiary & Quaternary Structure

Tertiary Structure:

- 3D folding of a single chain. Essential for function [REF Q8]. (`in Roboto Mono`)
- Stabilization:
  - **Hydrophobic:** Non-polar side chains cluster inside (core).
  - **Ionic:** Salt bridges between Acid/Base groups [REF Q39].
  - **Covalent:** Disulfide bridges (Cys-Cys).

Quaternary Structure:

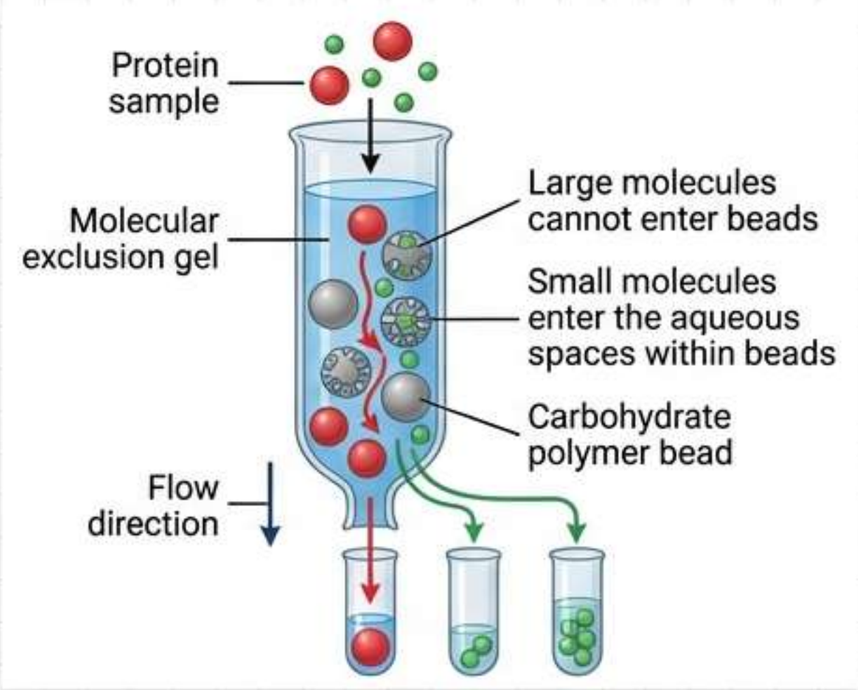
- Assembly of multiple subunits (protomers).
- **Example:** Hemoglobin ($\alpha_2\beta_2$). A Heteroprotein and Chromoprotein [REF Q34].



Methods: Chromatography Principles

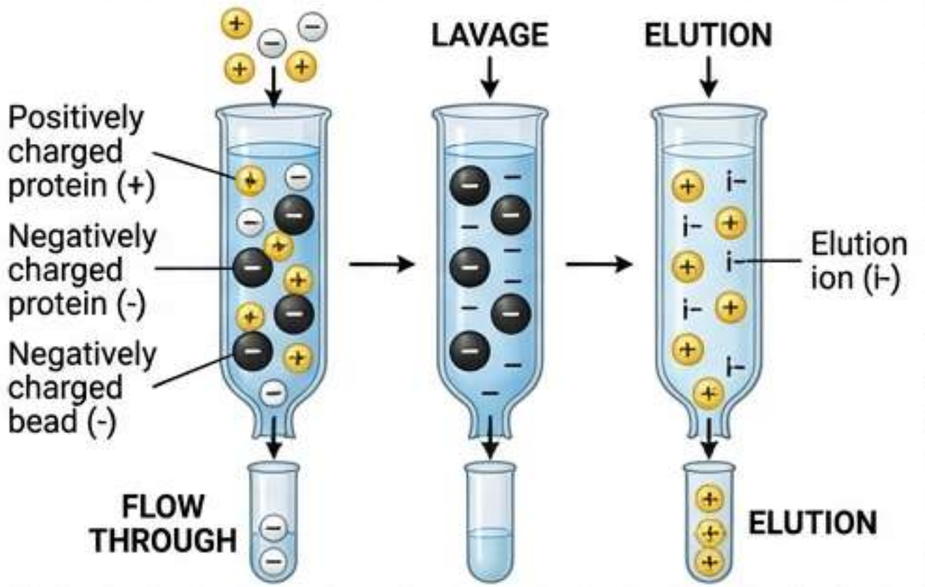
1. Gel Filtration (Exclusion):

- Separation by **SIZE**. Large molecules elute **FIRST** (cannot enter beads). Small molecules elute last.



2. Ion Exchange:

- Separation by **CHARGE**.
- **Cation Exchange (Neg beads):** Binds (+) proteins. Elute by increasing pH.
- **Order of Elution:** Lowest pI (Acidic) → Highest pI (Basic).
- *Example:* Asp → Leu → Lys [REF Q25].

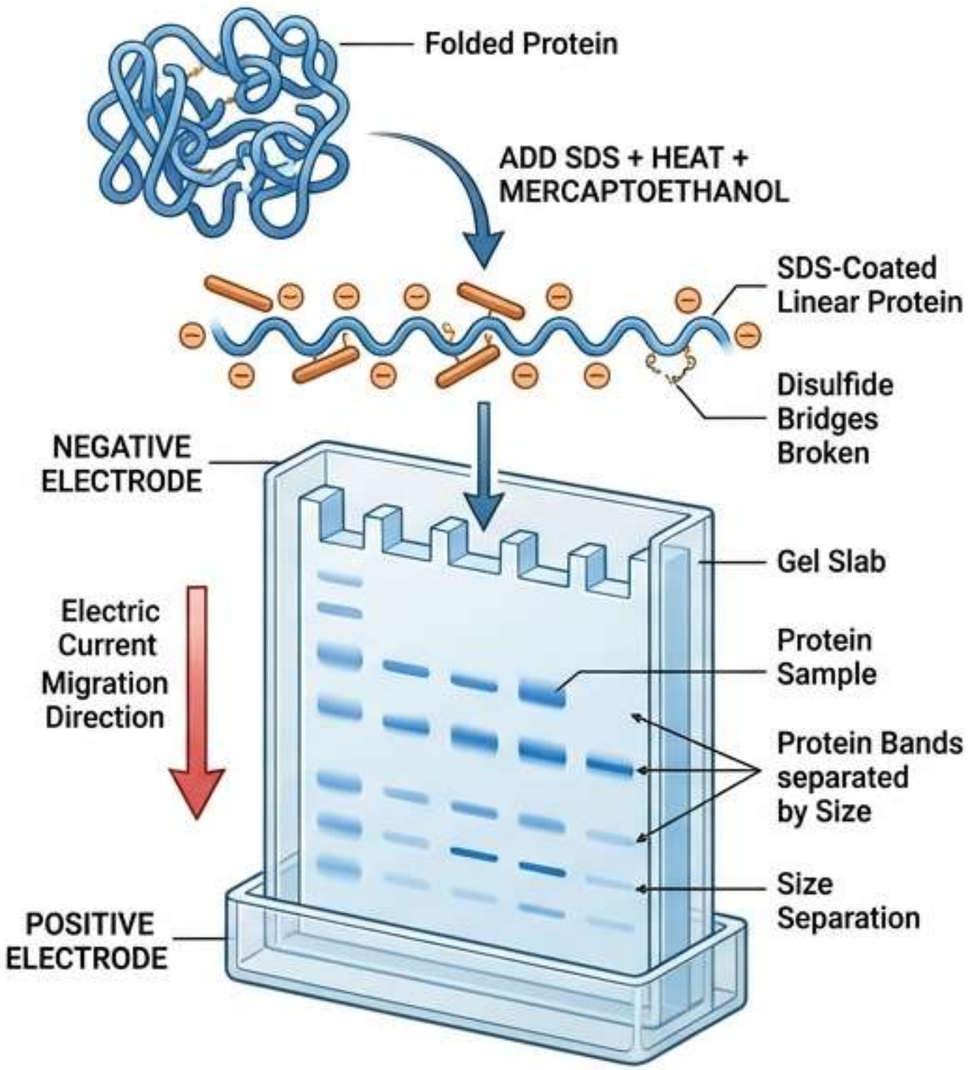


Methods: Electrophoresis & SDS-PAGE

1. **Zone Electrophoresis:**
   - Separates by Charge & Size.
   - **Serum Profile:** Albumin (fastest) → γ-globulins (slowest).

2. **SDS-PAGE (Denaturing):**
   - **SDS:** Anionic detergent unfolds protein + confers uniform negative charge.
   - **Mechanism**: Separation strictly by **MASS (Molecular Weight)**.
   - **Migration:** Small proteins migrate **faster**.
   - *Note:* Mercaptoethanol is added to break disulfide bridges [REF Q31].

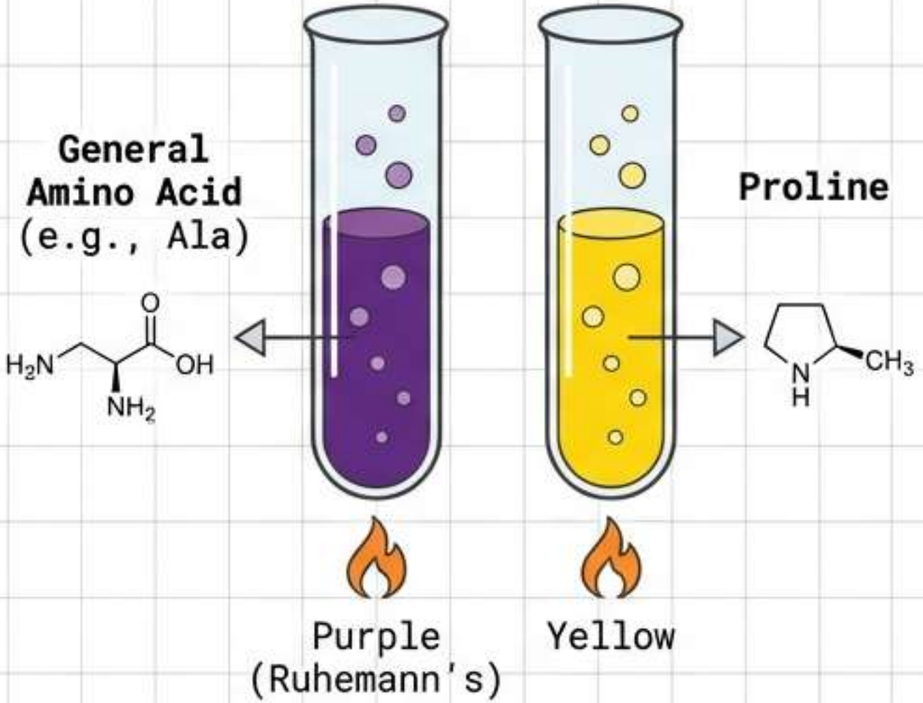
Exam Questions:
REF Q15/41: SDS-PAGE separates by mass, not charge.



Reactions & Identification

Detection:

- **Ninhydrin**: Reacts with α-NH2.
  - **Result**: Purple (Ruhemann's purple).
  - **Exception**: **Proline** (secondary amine) turns **YELLOW** [REF Q16-1].
- **Biuret**: Detects peptide bonds (Violet).



Sequencing:

- **Edman Degradation**: N-terminal sequencing.
- **Cyanogen Bromide (BrCN)**: Cleaves after **Methionine**.

REF Q29:
Acid hydrolysis destroys Tryptophan.

EXAM STRATEGY: Common Traps

Trap 1: Chirality

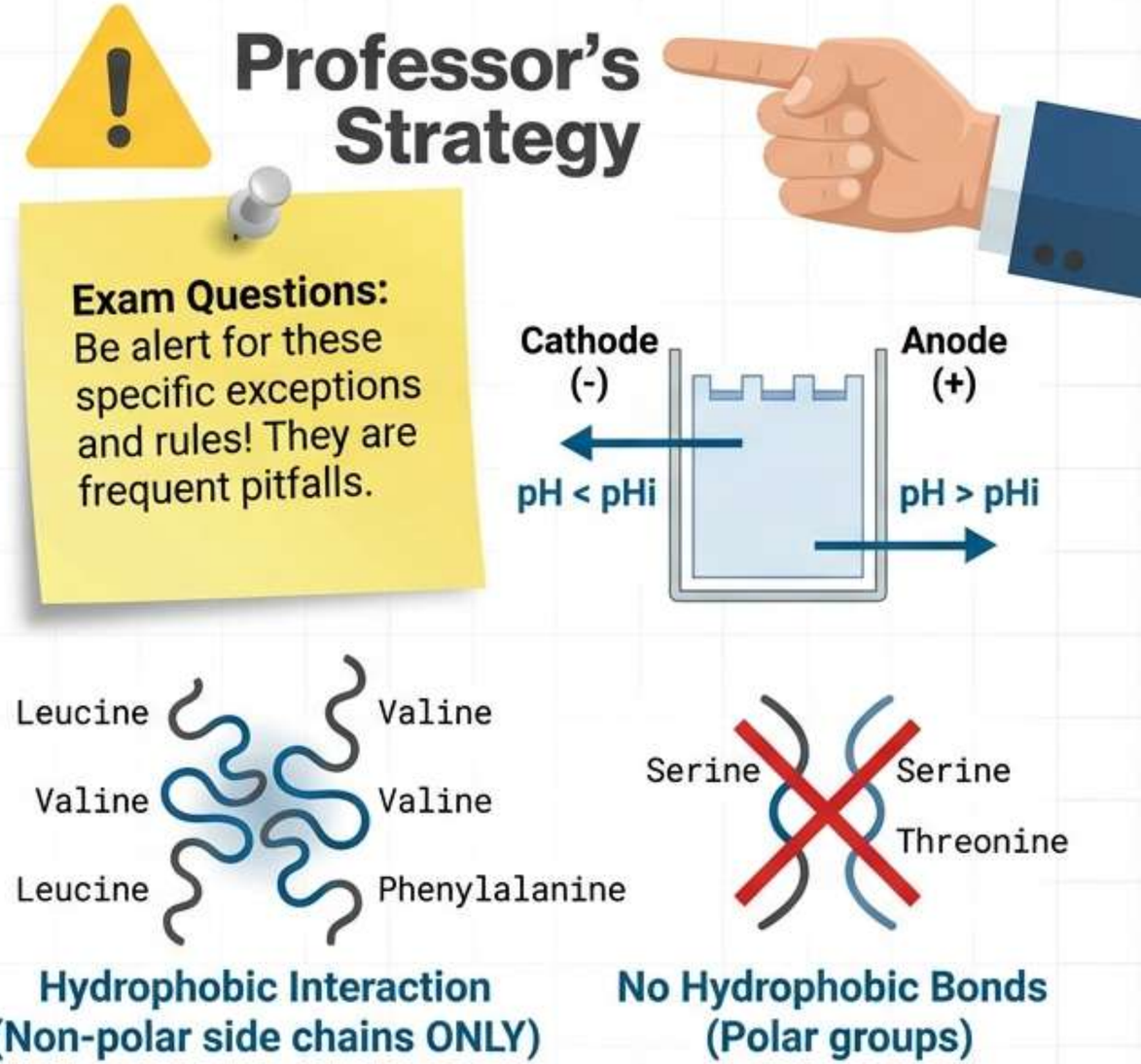
Question: "All amino acids are chiral."
Answer: FALSE. **Glycine** is **achiral.**

Trap 2: Migration Direction

Rule: If pH < pHi → Protein is (+), migrates to Cathode (-).
Rule: If pH > pHi → Protein is (-), migrates to Anode (+).

Trap 3: Hydrophobic Interactions

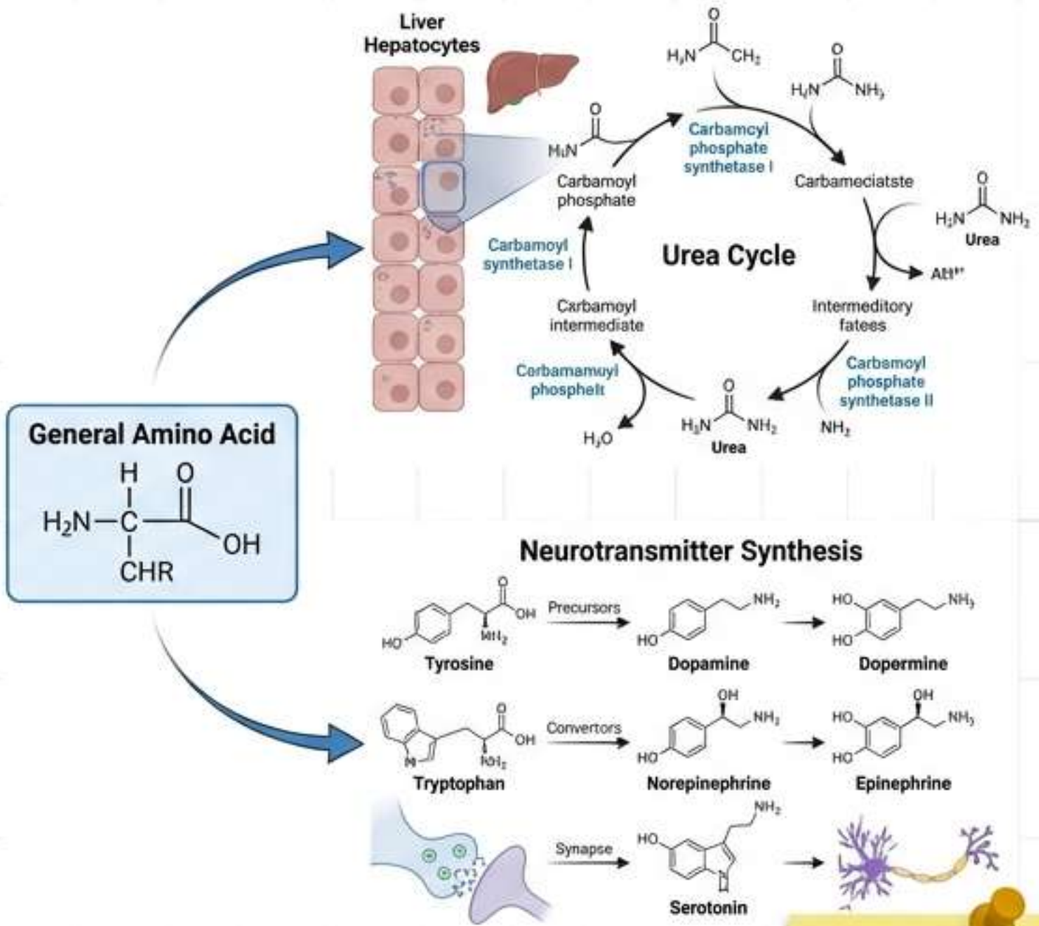
Question: "Hydrophobic bonds form between polar groups."
Answer: FALSE. Only between **non-polar** side chains.



Clinical Relevance & Summary

Why this matters:

* **Pathology**: Proteinuria (Kidney damage), Monoclonal Gammopathy (Spike in γ-globulins).
* **Metabolism**: Urea Cycle eliminates Nitrogen. Ketogenic/Glucogenic fates.



Final Review Checklist:

1. Memorize the **Non-Polar** list.
2. Master the **pHi Calculation** for Acidic/Basic AAs.
3. Know the **Separation Principles** (Charge vs Size).

EXAM QUESTIONS:
Be alert for these specific exceptions and rules! They are frequent pitfalls.