Amino acids

BIOS 1006

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Objectives

- Describe the properties of amino acids, in general (polar (hydrophilic) or nonpolar (hydrophilic), aliphatic or aromatic, basic (positive) or acidic (negative))
- Learn the names, abbreviations, adjectives, functional groups (structures) and properties of all 20 common α-amino acids (see the amino acids song)
- Identify the polar, hydrophobic, acidic or basic features in amino acid structures, and predict how two amino acid R-groups can interact
- Rationalize the position of each amino acid R-group on the hydropathy scale
- Describe the spectroscopic properties of amino acids (W and Y absorb UV light, W exhibits fluorescence, all absorb IR light, none absorb visible light)
- Know the pKa values of the R-groups (do not need to memorize), the average amino group (9.5) and the average carboxylic acid group (2.2)
- Determine the net charge of an amino acid or peptide at a specific pH (when pH $<$ pKa, the group is protonated; when pH $>$ pKa, the group is deprotonated)
- Calculate the pI values of amino acids and small peptides (take the average of flanking pKas - see "Calculating pI of a peptide")
- Draw the chemical structures of amino acid functional groups at different pHs (look at pKa, if it is less than pH then the H and a positive charge is lost, if it is greater than pH then the H is present)
- Extract pKa values from titration data (in the middle of the buffer region, pH = pKa)
- Describe the importance of a protein's pI in biological function
  - Least soluble at pI
  - Electrically neutral
  - No electrostatic interactions
- Describe the roles of amino acids in biological systems

- Building blocks of proteins
- Enzyme cofactors
- Hormones
- Neurotransmitters
- Metabolites
- Signaling molecules
- Energy sources
- Precursor molecules
- Intermediates in metabolic pathways
- Nutrient sources
- Buffers
- Transporters
- Receptors
- ...and a lot more

- Identify the amino acid from which amino acid derivatives are derived

Amino acids

Roles of amino acids

- Determine the structure of proteins
- Provide basis for protein function
- Signaling molecules
- Precursors for other biomolecules
- Intermediates in metabolic processes

Amino acid properties

- Zwitterionic (both positive and negative charges) and amphoteric (both an acid and a base) at pH 7
- Contains amino, hydrogen, carboxyl, and R-group (variant)
- Average molecular weight: 110 kDa
- α amino acids have 2 different stereoisomers (different arrangements) that are enantiomers (mirror images)
- Classified as D or L (in biological systems, L isomer is most common)
- Amino on the left = L, amino on the right = D
- Stereochemistry makes a big difference!

The amino acids

Functional groups found in amino acids

- Alcohols
- Thiols
- Thioethers
- Carboxylic acids
- Amides
- Basic groups

Classifications

Aromatic compounds are **flat rings**

Aliphatic are hydrocarbons that are not aromatic or planar, sp^3 hybridized **(straight, branched, cyclic)**.

Polar tyrosine, serine, threonine, cysteine, asparagine, glutamine, histidine, lysine, aspartic acid, glutamic acid.

Acidic and negative aspartate, glutamate

Basic and positive arginine, lysine, histidine

Glycine, G, Gly

Neither hydrophilic nor hydrophobic, R group is H (doesn't have α carbon), not chiral

Alanine, A, Ala

Hydrophobic, aliphatic. Methyl R group.

Valine, V, Val

Hydrophobic, aliphatic. Isopropyl R group.

Leucine, L, Leu

Hydrophobic, aliphatic. Isobutyl R group.

Isoleucine, I, Ile

Hydrophobic, aliphatic. 2-methylbutyl R group.

Proline, P, Pro

Hydrophobic, aliphatic. Cyclic structure, R group is attached to the amino group and the α carbon.

Methionine, M, Met

Hydrophobic, aliphatic. Contains sulfur, thioether R group (sulfur instead of oxygen).

Phenylalanine, F, Phe

Aromatic. Phenyl R group. (alanine with a phenyl group)

Tyrosine, Y, Tyr

Aromatic. Phenolic R group (hydroxyl group on the phenyl ring).

Tryptophan, W, Trp

Aromatic, two rings. Indole R group (nitrogen in the ring).

Histidine, H, His

Basic at neutrality, polar. Imidazole R group (two nitrogens in the ring).

Lysine, K, Lys

Basic at neutrality, polar. Amino R group.

Arginine, R, Arg

Basic at neutrality, polar. Guanidinium R group (three nitrogens).

Aspartate, D, Asp

Acidic at neutrality, polar. Carboxylate R group (carboxylic acid group $\rightarrow$ aspartic acid).

Glutamate, E, Glu

Acidic at neutrality, polar. Carboxylate R group (carboxylic acid group $\rightarrow$ glutamic acid).

Asparagine, N, Asn

Polar, uncharged. Amide R group.

Glutamine, Q, Gln

Polar, uncharged. Amide R group.

Serine, S, Ser

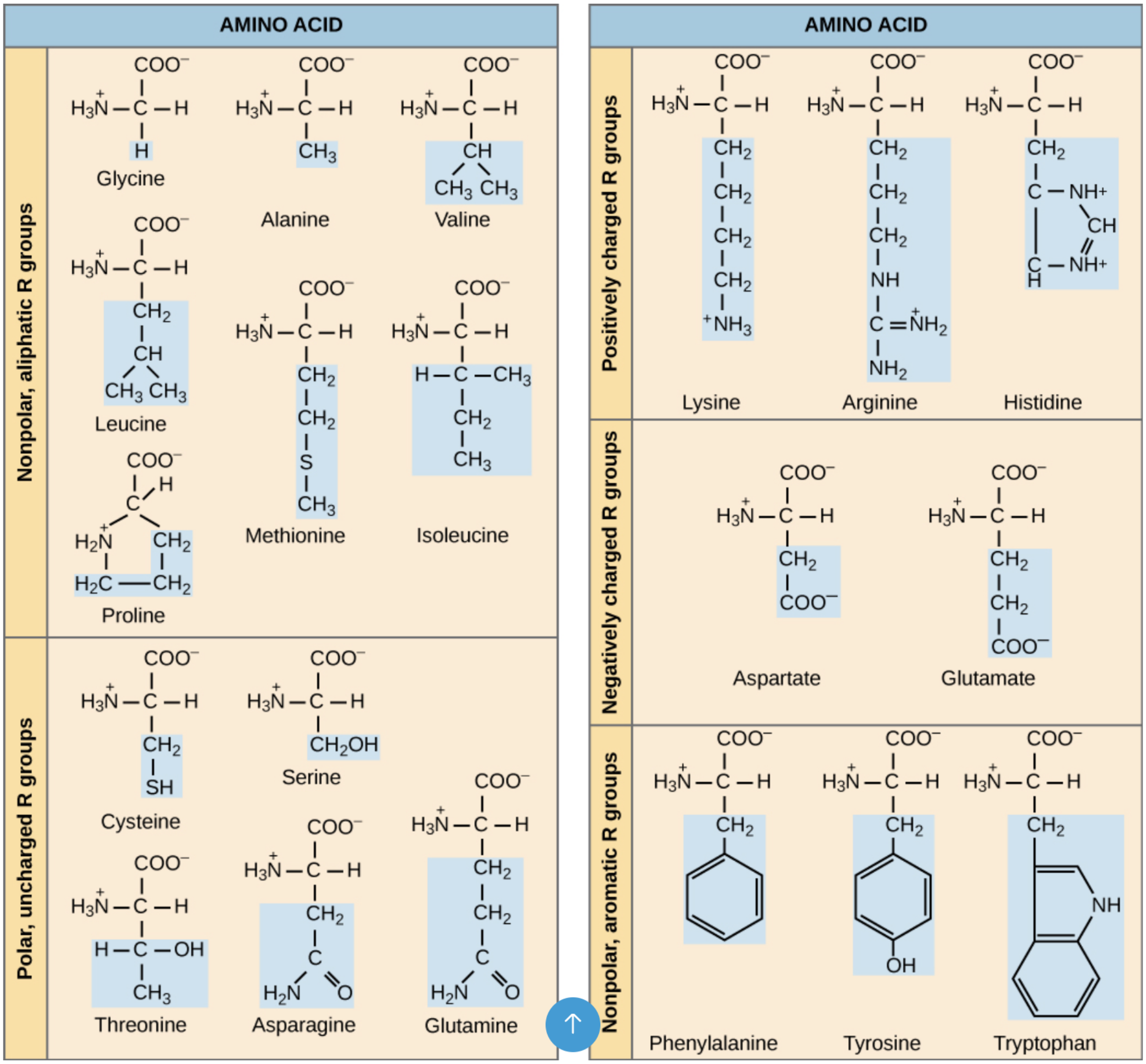
Polar, uncharged. Hydroxyl R group.

Threonine, T, Thr

Polar, uncharged. Hydroxyl R group (similar to serine, but with an additional methyl group).

Cysteine, C, Cys

Polar, uncharged. Thiol R group.



Spectroscopic properties

- No amino acids absorb the visible wavelengths
- Some residues absorb UV light (W,Y) and are uesd for protein structure determination
- All amino acids absorb at infrared wavelengths
- W also exhibits fluorescence

Acid base properties

pH = 1, protonated: both, net charge = +1

pH = 7, protonated: amino group, net charge = 0

pH = 13, protonated: neither, net charge = -1

Equivalence point = average of 2 flanking pKas

The isoelectric point (pI)

...is the pH at the equivalence point where the molecule has no net charge due to the ionization state of the molecule.

To calculate:

$$pI = \frac{pK_{a\,below} + pK_{a\,above}}{2} \tag{1}$$

Peptides

Amide or peptide bonds link amino acids together in proteins. (amine + carboxyl)

N-terminus at the amino group and C-terminus at the carboxyl group

pH vs. pKa

pKa is the dissociation constant of a weak acid, which is the pH at which half of the acid is dissociated. Half of it is in the protonated form (HA) and the other half is in the deprotonated form (A^-).

A higher Ka value indicates that an acid is stronger, and because the pKa is the negative logarithm of the Ka, a lower pKa value indicates a stronger acid.

Group Type	**pH < pKa**	**pH > pKa**
Acidic (e.g. $-COOH$, Asp, Glu)	Protonated (neutral)	Deprotonated (-1)
Basic (e.g. $-NH_3{}^+$, Lys, Arg, His)	Protonated ($+1$)	Deprotonated (neutral)

Calculating pI of a peptide

1. What is the charge at neutrality?
2. Arrange all pKa from lowest to highest.
3. Identify neutral form and find flanking pKas.
4. Calculate the average.

Example: Find the pI of this peptide at pH 7:

$$+\,H_3N\text{-A-G-R-K-N-I-M-}COO^-$$

A, G, N, I, M are not ionizable. R and K have a +1 charge. The two ends cancel out.

To find the pI: determine when the net charge = 0.

pH>pKa, so this is being deprotonated. However, we begin with assuming full protonation. COO^- gains a proton to become COOH, so that makes the overall charge +3.

Deprotonation occurs in this order (by pKa):

1. C-terminus pKa 2.2
2. N-terminus pKa 9.5
3. K side chain pKa 10.5
4. R side chain pKa 12.5

Now find where the charge is neutral:

(3+) 2.2 (2+) 9.5 (1+) 10.5 (0) 12.5 (1-)

The charge is neutral between 10.5 and 12.5. Take the average:

$$10.5 + 12.5 = 23$$

$$\frac{23}{2} = 11.5$$

The pI is $\boxed{11.5}$.