

Lecture 4-2 (9/14/20)

OUTLINE

Amino Acids

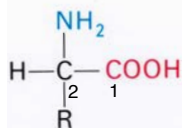
- Definition
- The 4 S's
- Common Properties
- Five Classes
 - Hydrophobic-aliphatic [6]
 - Hydrophobic-aromatic [3]
 - Special-sulfur [2]
 - Hydrophilic-polar [4]
 - Hydrophilic-charged [5]
- Other amino acids
- Linking amino acids
- Acid/base properties
 - Titrations
 - Isoelectric point
- Electrophoresis

Amino Acids: Building Blocks of Protein

Definition

- Proteins are linear heteropolymers of L- α -amino acids.
- These are organic acids with an amino group at the α -position, or the 2-position.

| | | | | | |
|------------|----------|----------|---------|----------|---------------------------|
| C | C | C | C | C | Functional |
| ϵ | δ | γ | β | α | Group (COO ⁻) |
| 6 | 5 | 4 | 3 | 2 | 1 |
- The amino group is basic and the carboxylate group is acidic (of course). The R-groups are different.



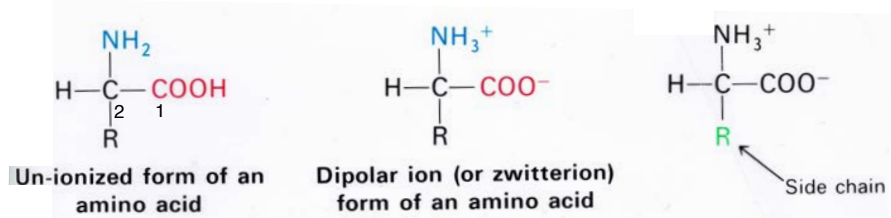
Un-ionized form of an amino acid

Amino Acids: Building Blocks of Protein

Definition

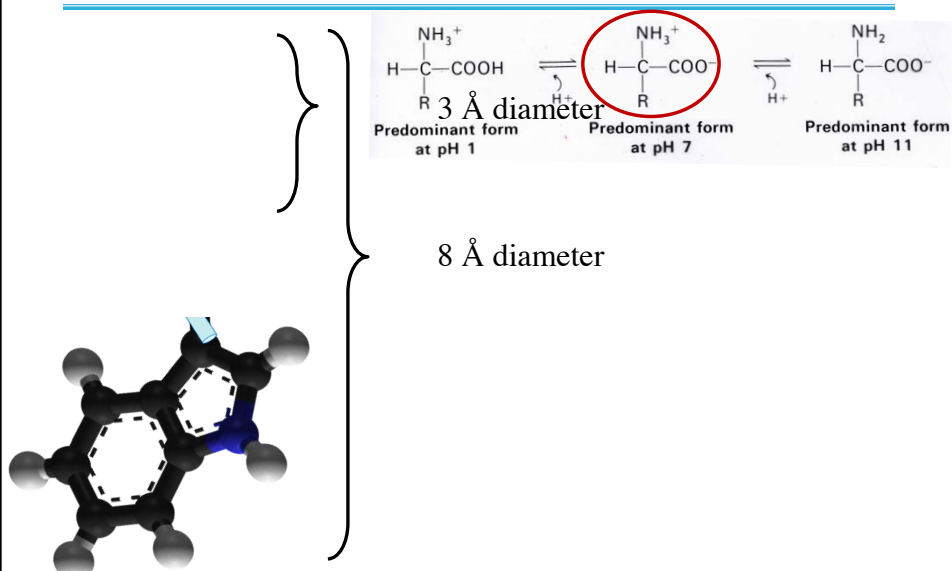
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The 4 S's: Size

Amino Acids: Building Blocks of Protein

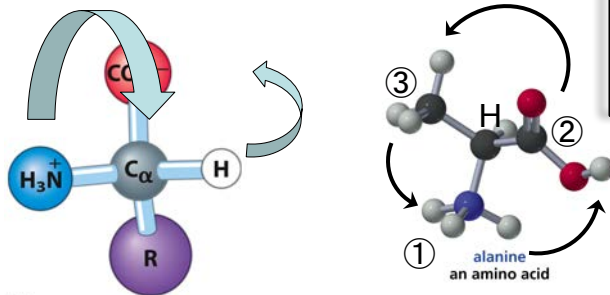


The 4 S's: Shape

Amino Acids: Building Blocks of Protein

Here we have to discuss stereochemistry: particularly what is meant by the "L" configuration
The "L" configuration means levorotary, or rotates polarized light counter-clockwise, or left handed

In R/S, this is what?



Recall:

Clockwise is R

Counterclockwise is S

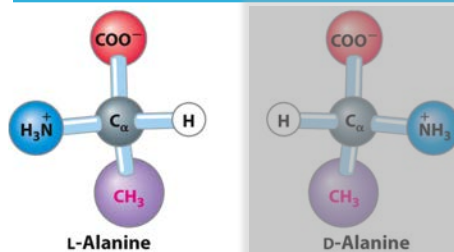
What is the relationship between R/S and D/L?

R = D

S = L

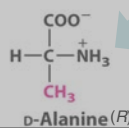
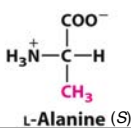
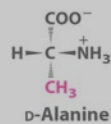
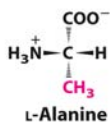
The 4 S's: Shape

Amino Acids: Building Blocks of Protein



L-Alanine

D-Alanine



Clockwise is R

Counterclockwise is S

R = D

S = L

Fisher Projection

1. Carbon chain vertical with functional group at top
2. At each carbon the vertical bonds to carbons are behind, projecting away from the viewer
3. At each carbon the horizontal bonds are projecting towards the viewer
4. If the functional group (not H) is to the left it's L
5. If the functional group (not H) is to the right it's D

The 4 S's: Stability

Amino Acids: Building Blocks of Protein

All amino acids are stable to acid, base, and heat

Exceptions are:

1. Trp (oxidation) → N-formyl-kynurenine
2. Cys (oxidation) → Disulfides (R'-S-S-R'')
3. Asn (deamination) → Hydrolysis of amide: Asp
4. Gln (deamination) → Hydrolysis of amide: Glu

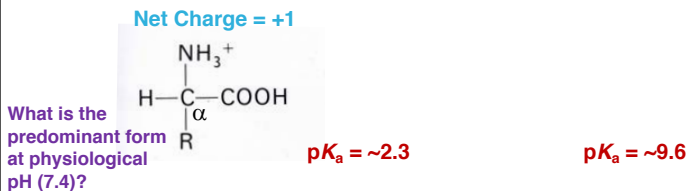
The 4 S's: Solubility

Amino Acids: Building Blocks of Protein

- As zwitterions, most amino acids are soluble to some degree. But, depending on the R group they are less soluble or more soluble
- The general grouping puts 10 as less soluble:
A, V, L, I, P, W, Y, F, M, C
- and 10 as more soluble:
G, S, T, N, Q, D, E, H, K, R

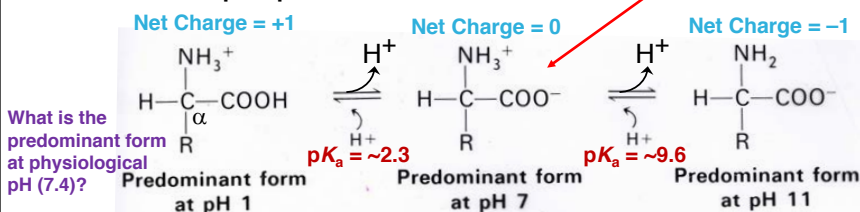
Amino Acids Have Three Common Properties

- Groups Attached to the α Carbon. The α carbon always has four substituents and is tetrahedral.
 - an **acidic** carboxyl group connected to the α carbon
 - a **basic amino** group (1° or 2°) connected to the α carbon
 - an α hydrogen connected to the α carbon
 - A fourth substituent called an “R group.”
- All Amino Acids are chiral with the L configuration (except glycine where the R-group is a hydrogen).
- Acid/Base properties: **Zwitterion**



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- Acid/Base properties: **Zwitterion**



Amino Acids: Classification

- The 20 amino acids found in proteins can be placed in five families based on the physical and chemical properties of their R groups:

- Hydrophobic, aliphatic (6)

Must KNOW

- Hydrophobic, aromatic (3)

- Special (hydrophobic/hydrophilic)(2)

- Hydrophilic, polar (4)

- Hydrophilic, charged (5)

Essential

Table:

| Name | 3-letter | 1-letter | Year discovered | % abundance in proteins | NOTES | Structure mnemonic device |
|------|----------|----------|-----------------|-------------------------|-------|---------------------------|
| ✓ | | | | | | |

Hydrophobic, aliphatic Amino Acids: Classification

| Name | 3-letter | 1-letter | Year discovered | % abundance in proteins | NOTES | Structure mnemonic device |
|--------------|----------|----------|-----------------|-------------------------|---|--|
| Glycine | Gly | G | 1820 | 7 | <i>Smallest, not chiral</i> | <i>H</i> |
| Alanine | Ala | A | 1888 | 8 | <i>Foundational for ~10 other AA</i> | <i>Methyl</i> |
| Valine ✓ | Val | V | 1856 | 7 | <i>isopropyl</i> | <i>V-shaped</i> |
| Leucine ✓ | Leu | L | 1819 | 10 | <i>Most abundant, dominant</i> | <i>Ala + Val</i> |
| Isoleucine ✓ | Ile | I | 1904 | 6 | <i>Two chiral centers (L & D)</i> | <i>Val + Me</i> |
| Proline | Pro | P | 1901 | 5 | <i>Only imino acid (2° amine); special bonds in proteins; is modified by hydroxyl</i> | <i>5-membered ring; same #C's as Val</i> |

Hydrophobic, aliphatic Amino Acids: Classification

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\ | \\ \text{H} \end{array}$$

Gly

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\ | \\ \text{CH}_3 \end{array}$$

Ala

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\ | \\ \text{CH} \\ / \quad \backslash \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$$

Val

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\ | \\ \text{CH}_2 \\ | \\ \text{CH} \\ / \quad \backslash \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$$

Leu

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+-\text{C}-\text{H} \\ | \\ \text{H}-\text{C}-\text{CH}_3 \\ | \\ \text{CH}_2 \\ | \\ \text{CH}_3 \end{array}$$

Ile

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_2\text{N}^+-\text{C}-\text{H} \\ | \\ \text{H}_2\text{C}-\text{CH}_2 \\ | \\ \text{CH}_2 \end{array}$$

Pro

Gavlip family

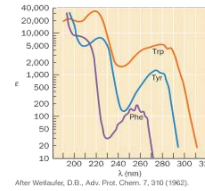
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- The 20 amino acids found in proteins can be placed in five families based on the physical and chemical properties of their R groups:
 - Hydrophobic, aliphatic (6) Gavlip family
 - Hydrophobic, aromatic (3)
 - Special (hydrophobic/hydrophilic)(2)
 - Hydrophilic, polar (4)
 - Hydrophilic, charged (5)

Hydrophobic, aromatic Amino Acids: Classification

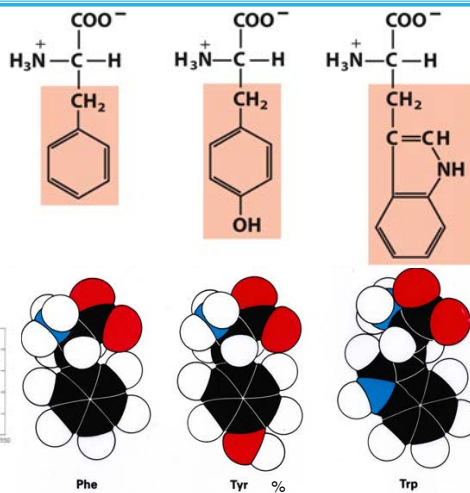
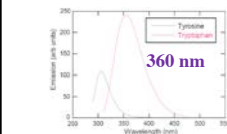
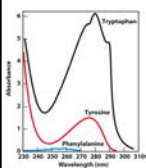
Recall:



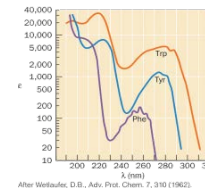
| Name | 3-letter | 1-letter | Year discovered | abundance in proteins | NOTES | pK_a | Structure mnemonic device |
|---------------|----------|----------|-----------------|-----------------------|---|----------------|---------------------------|
| Phenylalanine | ✓Phe | F | 1879 | 4 | <i>aromatic</i> <i>Absorb UV light</i> <i>aromatic & fluorescent</i> <i>least abundant, largest AA</i> | ≈ 10.1 | Phenyl+Ala |
| Tyrosine | Tyr | Y | 1846 | 3 | | | |
| Tryptophan | ✓Trp | W | 1901 | 1 | | | |

Hydrophobic, aromatic Amino Acids: Classification

PTT family (push-to-talk)



Recall:



Absorb UV light

| λ_{max} | Extinction coefficient ($\times 10^{-3}$) |
|------------------------|---|
| 259 | 0.7 |
| 278 | 1.1 |
| 279 | 5.2 |

| Name | 3-letter | 1-letter | Year discovered | abundance in proteins | NOTES | pK_a | Structure mnemonic device |
|---------------|----------|----------|-----------------|-----------------------|--|----------------|---------------------------|
| Phenylalanine | ✓Phe | F | 1879 | 4 | <i>aromatic</i> <i>aromatic, can ionize; amphipathic</i> <i>aromatic & fluorescent; least abundant</i> | ≈ 10.1 | Phenyl+Ala |
| Tyrosine | Tyr | Y | 1846 | 3 | | | |
| Tryptophan | ✓Trp | W | 1901 | 1 | | | |

Amino Acids: Classification

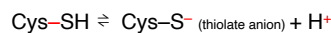
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Special (Sulfur) Amino Acids: Classification

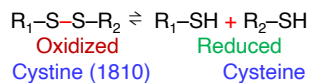
Hydrophobic
/Hydrophilic (Cys)

| AA | Hydropathy index (ΔG) |
|-----|---------------------------------|
| Ile | 4.5 |
| Val | 4.2 |
| Leu | 3.8 |
| Phe | 2.8 |
| Tyr | -1.3 |
| Met | 1.9 |
| Cys | 2.5 |

- Cysteine can ionize:



- Cysteine can form disulfide bonds:



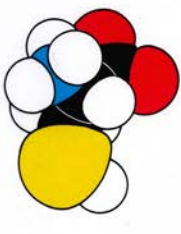
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| Methionine ✓ | Met | M | 1922 | 2 | Most like straight-chain aliphatic | | Ala+Me/ether |
| Cysteine | Cys | C | 1899 | 2 | can ionize; nucleophile | 10.5 | Ala+SH (thiol) |

Special (Sulfur) Amino Acids: Classification

Hydrophobic /Hydrophilic (Cys)

$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+ - \text{C} - \text{H} \\ | \\ \text{CH}_2 \\ | \\ \text{SH} \end{array}$$

Cys



$$\begin{array}{c} \text{COO}^- \\ | \\ \text{H}_3\text{N}^+ - \text{C} - \text{H} \\ | \\ \text{CH}_2 \\ | \\ \text{CH}_2 \\ | \\ \text{S} \\ | \\ \text{CH}_3 \end{array}$$

Met

MC family
(master of ceremony)

- Cysteine can ionize:
 $\text{Cys-SH} \rightleftharpoons \text{Cys-S}^- \text{ (thiolate anion)} + \text{H}^+$
- Cysteine can form disulfide bonds:
 $\text{R}_1\text{-S-S-R}_2 \rightleftharpoons \text{R}_1\text{-SH} + \text{R}_2\text{-SH}$
Oxidized Reduced
Cystine (1810) Cysteine

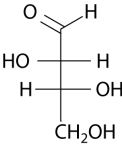
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Hydrophilic, polar

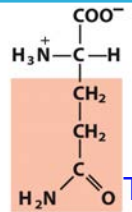
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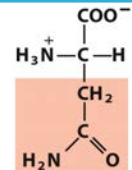
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| Asparagine | Asn | N | 1806 | 4 | <i>Asx</i> ; gets hydrolyzed to <i>Asp</i> | Amide of <i>Asp</i> |
| Serine | Ser | S | 1865 | 7 | Isolated from Sericin, polar cousin of <i>Ala</i> | hydroxyl+ <i>Ala</i> |
| Threonine ✓ | Thr | T | 1935 | 6 | Two chiral centers (<i>L</i> & <i>D</i>) | <i>Me</i> + <i>Ser</i> |

Hydrophilic, polar

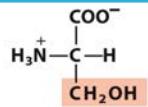
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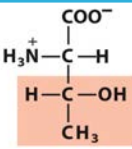
Gln



Asn

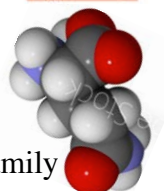


Ser

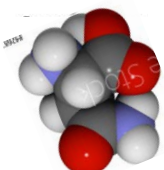


Thr

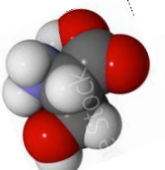
These amino acids side chains can form hydrogen bonds.



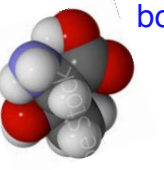
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