- Reading: Ch3; 70-76
- Homework #4 (due this Sunday)

Lecture 4 (9/13/24)

NEXT

- Reading: Ch3; 76–82, 87–89
- Homework #5

OUTLINE

Amino Acids

- Definition, Structure, and Properties
  - The 4 S's
  - Common Properties
  - Five Classes
    - Hydrophobic–aliphatic [6]
    - Hydrophobic–aromatic [3]
    - Special–sulfur [2]
    - Hydrophilic–polar [4]
    - Hydrophilic–charged [5]

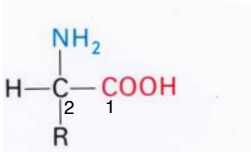
Amino Acids: Building Blocks of Protein

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

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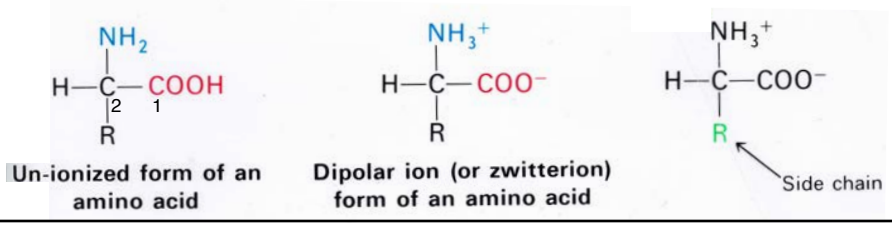
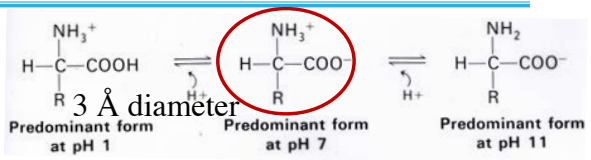


The 4 S's: Size

Amino Acids: Building Blocks of Protein



3 Å diameter

8 Å diameter

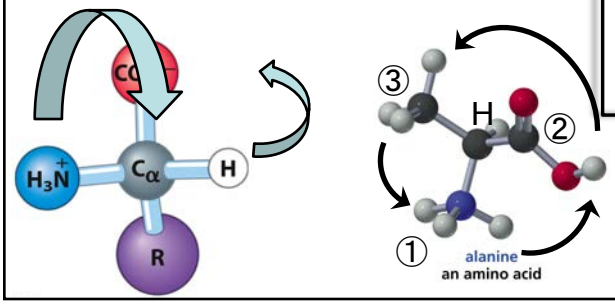
The 4 S's: Shape

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

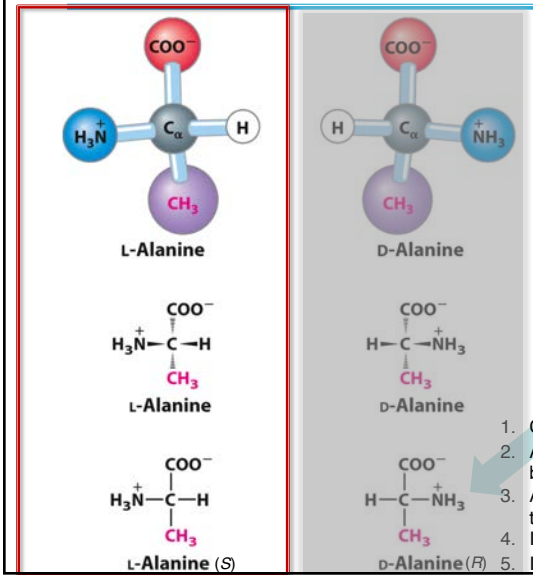
In R/S, this is what?

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



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

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

Exceptions are:

1. Tryptophan (oxidation) →N-formyl-kynurenine
2. Cysteine (oxidation) →Disulfides (R'-S–S-R")
3. Asparagine (deamination) →Hydrolysis of amide: Asp
4. Glutamine (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:

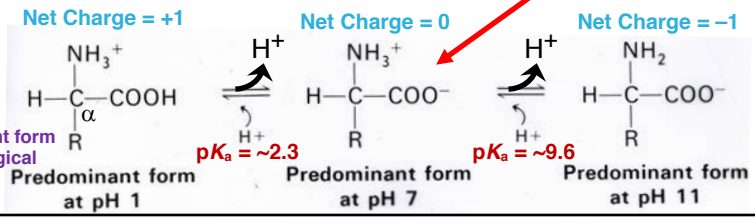
  A, V, L, I, P, W, Y, F, M, C
- and 10 as more soluble:

  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



What is the predominant form at physiological pH (7.4)?

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)
  - Hydrophobic, aromatic (3)
  - Special (hydrophobic/hydrophilic)(2)
  - Hydrophilic, polar (4)
  - Hydrophilic, charged (5)

Must KNOW:
Name
3-letter abbrev.
1-letter abbrev.
recognize and
draw the structure,
including the charge

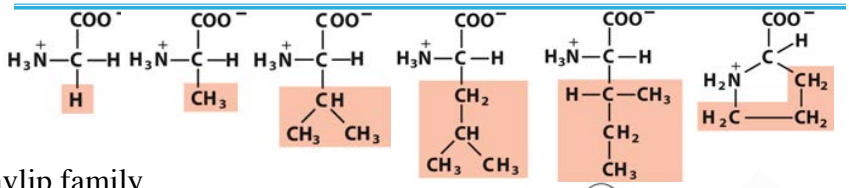
Essential

Table:

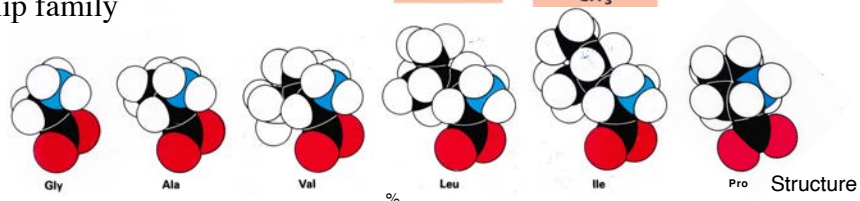
Name ✓	3-letter	1-letter	Year discovered	% abundance in proteins	NOTES	Structure mnemonic device

Hydrophobic, aliphatic

Amino Acids: Classification



Gavlip family



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

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:
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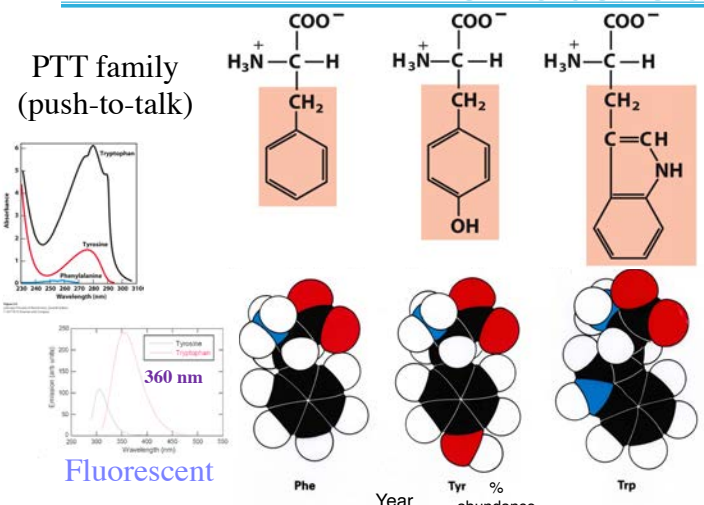
  - Hydrophilic, charged (5)

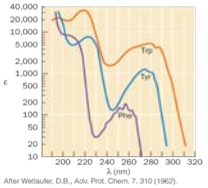
Hydrophobic, aromatic

Amino Acids: Classification

PTT family
(push-to-talk)



Recall:



Fluorescent

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	*aromatic*		*Phenyl+Ala*
Tyrosine	Tyr	Y	1879	3	*aromatic, can ionize; $pK_a \approx 10.1$ amphipathic*		*p-phenol+Ala*
Tryptophan ✓	Trp	W	1901	1	*aromatic & fluorescent; least abundant*		*Indole+Ala*

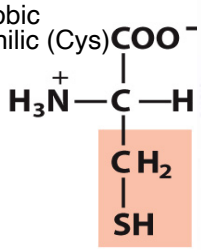
Amino Acids: Classification

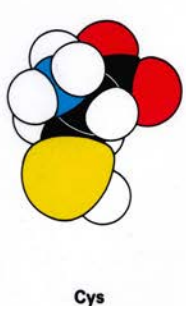
- The 20 amino acids found in proteins can be placed in five families based on the physical and chemical properties of their R groups:
  - Hydrophobic, aliphatic (6) — Gavlip family
  - Hydrophobic, aromatic (3) — PTT family
  - Special (hydrophobic/hydrophilic)(2)
  - Hydrophilic, polar (4)
  - Hydrophilic,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

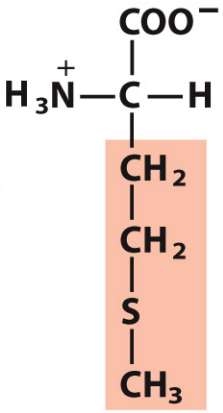
Amino Acids: Classification

Special (Sulfur)

Hydrophobic /Hydrophilic (Cys)







MC family
(master of ceremony)

- Cysteine can ionize:

$$Cys\text{–}SH \rightleftharpoons Cys\text{–}S^{-}\ (\text{thiolate anion}) + H^{+}$$

- Cysteine can form disulfide bonds:

$$R_1\text{–}S\text{–}S\text{–}R_2 \rightleftharpoons R_1\text{–}SH + R_2\text{–}SH$$

Oxidized Cystine (1810) ⇌ Reduced Cysteine

Name	3-letter	1-letter	Year discovered	% abundance in proteins	NOTES	pK_a	Structure mnemonic device
Methionine ✓	Met	M	1922	2	*Most like straight-chain aliphatic*		*Ala+Me/ether*
Cysteine	Cys	C	1899	2	*can ionize; nucleophile* (Cα is *R*)	*10.5*	*Ala+SH*