Amino acids

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Resources

- This lecture
- Campbell and Farrell’s Biochemistry, Chapters 3 (pp.66-76)
The amino acids that occur in proteins naturally are all of the L form.
Side-chain carbon atoms are designated with letters of the Greek alphabet, counting from the $\alpha$-carbon. These carbon atoms are, in turn, the $\beta$-, $\gamma$-, $\delta$-, and $\varepsilon$-carbons.

The terminal carbon atom is referred to as the $\omega$-carbon.
Types of amino acids

There are twenty kinds of amino acids depending on the side chains varying in:

- Size
- Shape
- Charge
- Hydrogen-bonding capacity
- Hydrophobic character
- Chemical reactivity
## Classification (according to R group)

<table>
<thead>
<tr>
<th>Non-polar</th>
<th>Polar</th>
<th>Charged (positive)</th>
<th>Charged (negative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>Serine</td>
<td>Lysine</td>
<td>Glutamate</td>
</tr>
<tr>
<td>Valine</td>
<td>Threoeine</td>
<td>Arginine</td>
<td>Aspartate</td>
</tr>
<tr>
<td>Leucine</td>
<td>Glutamine</td>
<td>Histidine</td>
<td></td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Asparagine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mehionine</td>
<td>Cysteine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Tyrosine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenylalanine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycine</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Glycine

Is it chiral?
Non-polar, aliphatic amino acids
Alanine

\[ +H_3N-CH_3-C-COO^- \]

(Ala, A)
Valine, leucine, and isoleucine

These are essential amino acids in the sense that the body cannot synthesize them.
Methionine

\[
\text{CH}_3 \quad \text{S} \quad \text{CH}_2 \\
\text{CH}_2 \quad \text{+H}_3\text{N} \quad \text{C} \quad \text{COO}^- \quad \text{H}
\]

Methionine (Met. M)
Proline (imino acid)

Secondary nitrogen
Polar amino acids
Glycine

Is it chiral?
Serine and threonine

Serine (Ser, S)

+H₃N—C—COO⁻

H

CH₂

OH

Alanine (Ala, A)

+H₃N—C—COO⁻

CH₃

H

Threonine (Thr, T)

+H₃N—C—COO⁻

H

Valine (Val, V)

CH₃

CH₃

+H₃N—C—COO⁻
Cysteine (Cys, C)

Thiol group
Asparagine and glutamine

Amide groups

Asparagine (Asn, N)

Glutamine (Gln, Q)
Aromatic amino acids
Phenylalanine, tyrosine, Tryptophan
Positively-charged amino acids
Lysine and arginine

Lysine (Lys, K)

Arginine (Arg, R)

guanidino group
Histidine

\[
\text{Histidine (His, H)}
\]

\[
\text{Imidazole}
\]
Negatively-charged amino acids
Aspartic acid and glutamic acid

Aspartate (Asp, D)  Glutamate (Glu, E)
Questions

1. Two amino acids are negatively-charged:

2. The following amino acid is achiral:

3. ...etc.
Specialized and uncommon amino acids
Biological significance of amino acids

α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds:

- Hormones
- Neurotransmitters
- Biologically active peptides

Amino acid pool

Body protein

Synthesis of:
- Porphyrins
- Creatine
- Neurotransmitters
- Purines
- Pyrimidines
- Other nitrogen-containing compounds

Glucose, glycogen

Ketone bodies, fatty acids, steroids

CO₂
Tyrosine (1)

- It is converted into **catecholamine** neurotransmitters
  - Dopamine
  - Norepinephrine
  - Epinephrine
- **flight or fight**
Tyrosine (2)

- Tyrosine is converted into
  - Melanin (skin color)
  - Thyroxine (hormone)
Cheese contain high amounts of tyramine, which mimics epinephrine; for many people a cheese omelet in the morning is a favorite way to start the day.
Tryptophan serves as the precursor for the synthesis of Neurotransmitters

- **Serotonin** (neurotransmitter-sedative)
- **Melatonin** (day-night cycle)
Histamine

- Regulates physiological function in the gut
- Acts as a neurotransmitter
- Causes allergic symptoms (a major cause for asthma)
- Contributes to inflammatory response
- Causes constriction of smooth muscle
Glutamate

- Is a precursor of $\gamma$-aminobutyric acid (GABA)
- Inhibitory neurotransmitter (CNS)
γ-carboxyglutamate (Gla)

- The glutamate residues of some clotting factors are carboxylated to form γ-carboxyglutamate (Gla) residues.
- Vitamin K is essential for the process.
- This carboxylation is essential for the function of the clotting factors.
L-arginine is the precursor of nitric oxide (NO)

NO functions:
- Vasodilation, inhibition of platelet adhesion, inhibition of leukocyte adhesion, antiproliferative action, scavenging superoxide anion (anti-inflammatory)
Lysine and proline

Both are hydroxylated and are part of collagen structure.
Ionization of amino acids
Why do amino acids get ionized?

- carboxyl group
- negative charge
- acid (proton donor)
- amino group
- positive charge
- base (proton acceptor)
Zwitterion and isoelectric point

- At physiological pH, amino acids (without ionizable groups) are electrically neutral
- Zwitterion: a molecule with two opposite charges and a net charge of zero

\[
\begin{align*}
\text{NH}_3^+ & \\
\text{R-CH-} & \\
\text{COO}^- & \\
\text{a zwitterion}
\end{align*}
\]
Effect of pH

Isoelectric zwitterion

\[
\begin{align*}
\text{H}_3\text{N}^+ - &\quad \text{C} - &\quad \text{H} &\quad \text{R} \\
\text{COOH} &\quad &\quad &\quad \\
&\quad \overset{\text{H}^+}{\text{pK}_a = 2.34} &\quad \text{H}_3\text{N}^+ - &\quad \text{C} - &\quad \text{H} &\quad \text{R} \\
&\quad &\quad &\quad \\
H_2\text{N} &\quad &\quad &\quad \text{C} - &\quad \text{H} &\quad \text{R} \\
&\quad &\quad &\quad &\quad \text{COO}^- &\quad \\
\end{align*}
\]
Example 1 (alanine)

$$\text{pH} = pK_a + \log \frac{\text{conjugate base}}{\text{weak acid}}$$
The pH where the net charge of a molecule such as an amino acid or protein is zero is known as the isoelectric point or pI.

For the nonpolar and polar amino acids with two pKa’s, the isoelectric point is calculated by taking the numerical average of the carboxyl group pKa and the α-amino group pKa.

\[ pI = \frac{pK_{a1} + pK_{a2}}{2} \]
Nine of the 20 amino acids have ionizable side chains.

These amino acids are tyrosine, cysteine, arginine, lysine, histidine, serine, threonine, and aspartic and glutamic acids.

Each side chain has its own pKa values for ionization of the side chains.
### pl of amino acids

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Side Chain pKₐ³</th>
<th>pl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine</td>
<td>12.5</td>
<td>10.8</td>
</tr>
<tr>
<td>Aspartic Acid</td>
<td>4.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Cysteine</td>
<td>8.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Glutamic Acid</td>
<td>4.1</td>
<td>3.2</td>
</tr>
<tr>
<td>Histidine</td>
<td>6.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Lysine</td>
<td>11.0</td>
<td>10</td>
</tr>
</tbody>
</table>

Let’s consider pKa of -NH₂ = 9 and pKa of –COOH = 2 for all amino acids.
Calculation of pI of amino acids with ionizable R groups

The isoelectric point for these amino acids is calculated by taking the average of the pKa’s of the groups with same charge when ionized.

In this case, the total charge on the groups with like charge must equal one (1) so that it can be balanced by the one (1) opposite charge present on the molecule.
Example: Glutamate

To calculate the isoelectric point of Glu, the pKa’s of the two carboxyl groups are averaged.
Histidine

\[ pI = \sim 7.5 \] (The imidazole group can be uncharged or positively charged near neutral pH).
1. Draw the titration curve of histidine.

2. What is the ratio of conjugate base/acid of glutamate at pH 4.5?

3. What is the total charge of lysine at pH 7?
What do you need to know?

- The names of amino acids
- The special structural features of amino acids
- Their abbreviations or designations
- The uncommon amino acids, their precursor and function (if any)
- The pKa of groups
  - not exact numbers, but which ones are acidic, basic, or near neutral