Amino Acids and Peptides

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Protein structure and function

- Greek: proteios, primary (importance)
- 50% of body’s dry weight is protein
- Wide range of different functions
- Polymers of amino acids
- Structure of the amino acids

<table>
<thead>
<tr>
<th>TYPE</th>
<th>FUNCTION</th>
<th>EXAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzymes</td>
<td>Catalysts</td>
<td>Amylase—begins digestion of carbohydrates by hydrolysis</td>
</tr>
<tr>
<td>Hormones</td>
<td>Regulate body functions by carrying messages to receptors</td>
<td>Insulin—facilitates use of glucose for energy generation</td>
</tr>
<tr>
<td>Storage proteins</td>
<td>Make essential substances available when needed</td>
<td>Myoglobin—stores oxygen in muscles</td>
</tr>
<tr>
<td>Transport proteins</td>
<td>Carry substances through body fluids</td>
<td>Serum albumin—carries fatty acids in blood</td>
</tr>
<tr>
<td>Structural proteins</td>
<td>Provide mechanical shape and support</td>
<td>Collagen—provides structure to tendons and cartilage</td>
</tr>
<tr>
<td>Protective proteins</td>
<td>Defend the body against foreign matter</td>
<td>Immunoglobulin—aids in destruction of invading bacteria</td>
</tr>
<tr>
<td>Contractile proteins</td>
<td>Do mechanical work</td>
<td>Myosin and actin—govern muscle movement</td>
</tr>
</tbody>
</table>

The alpha carbon is the central carbon in an amino acid to which the amine, carboxyl and side chain R groups attach.

An α-amino acid
What should not be forgotten for good?

- There are a lot of amino acids in life.
- There are 20 encoded by the genetic code.
- Their general structure (amino, carboxyl, H, R), the basis of their classification.
- Two vs. 3-dimensional (handedness, chirality, chiral vs. achiral, left vs. right, L vs. D).
## Names and codes

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>3-letter code</th>
<th>1-letter code</th>
<th>Amino Acid</th>
<th>3-letter code</th>
<th>1-letter code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>Ala</td>
<td>A</td>
<td>Leucine</td>
<td>Leu</td>
<td>L</td>
</tr>
<tr>
<td>Arginine</td>
<td>Arg</td>
<td>R</td>
<td>Lysine</td>
<td>Lys</td>
<td>K</td>
</tr>
<tr>
<td>Asparagine</td>
<td>Asn</td>
<td>N</td>
<td>Methionine</td>
<td>Met</td>
<td>M</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>Asp</td>
<td>D</td>
<td>Phenylalanine</td>
<td>Phe</td>
<td>F</td>
</tr>
<tr>
<td>Cysteine</td>
<td>Cys</td>
<td>C</td>
<td>Proline</td>
<td>Pro</td>
<td>P</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>Glu</td>
<td>E</td>
<td>Serine</td>
<td>Ser</td>
<td>S</td>
</tr>
<tr>
<td>Glutamine</td>
<td>Gln</td>
<td>Q</td>
<td>Threonine</td>
<td>Thr</td>
<td>T</td>
</tr>
<tr>
<td>Glycine</td>
<td>Gly</td>
<td>G</td>
<td>Tryptophan</td>
<td>Trp</td>
<td>W</td>
</tr>
<tr>
<td>Histidine</td>
<td>His</td>
<td>H</td>
<td>Tyrosine</td>
<td>Tyr</td>
<td>Y</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Ile</td>
<td>I</td>
<td>Valine</td>
<td>Val</td>
<td>V</td>
</tr>
</tbody>
</table>
Charged

Aspartic acid (Asp, D)

Glutamic acid (Glu, E)

Histidine (His, H)

Arginine (Arg, R)

Lysine (Lys, K)
Polar, Uncharged

Serine (Ser, S)

Threonine (Thr, T)

Asparagine (Asn, N)

Cysteine (Cys, C)

Glutamine (Gln, Q)

Tyrosine (Tyr, Y)
Non-polar, Uncharged

Glycine (Gly, G)

Alanine (Ala, A)

Valine (Val, V)

Proline (Pro, P)

Leucine (Leu, L)

Isoleucine (Ile, I)

Methionine (Met, M)

Tryptophan (Trp, W)

Phenylalanine (Phe, F)
Amino acids – general structure

The amino acids obtained by hydrolysis of proteins differ in respect to $R$ (the side chain).

The properties of the amino acid vary as the structure of $R$ varies.
Glycine is the simplest amino acid. It is the only one that is achiral.

In all of the other amino acids the α-carbon is a stereogenic center.
Alanine

(Ala or A)
Valine

(Val or V)
Leucine

\[
\begin{align*}
\text{H}_3\text{N} & \quad \text{C} \quad \text{C} \quad \text{O} \\
& \quad \text{H} \quad \text{O} \\
& \quad \text{CH}_2\text{CH(CH}_3\text{)}_2
\end{align*}
\]

Leucine

(Leu or L)
Isoleucine

Isoleucine

(lle or I)
Methionine

(Met or M)
Phenylalanine

(Phe or F)
Tryptophan

\[
\begin{align*}
&\text{H}_3\text{N} + \text{C} = \text{C} = \text{C} + \text{O} \\
&\text{CH}_2
\end{align*}
\]

(Trp or W)
Asparagine

\[
\text{H}_3\text{N} + \overset{\text{H}}{\text{C}} \overset{\text{+}}{\text{C}} \overset{\text{O}}{\text{O}} \overset{\text{=}}{\text{H}}_2\text{NCH}_2\text{CCH}_2\text{O} \\
\text{Asparagine} \\
\text{(Asn or N)}
\]
Glutamine

\[
\text{H}_3\text{N} - \text{C} - \text{C} - \text{O} - \\
\text{H}_2\text{NCOCH}_2\text{CH}_2
\]
Serine

(Ser or S)
Threonine

H₃N + \[\text{CH}_3\text{CHOH}\] + \[\text{C} \quad \text{C} \quad \text{O}\] = Threonine

(Thr or T)
Aspartic Acid

(Asp or D)
Glutamic Acid

Glutamic Acid

(Glu or E)
Tyrosine

\[
\text{H}_3\text{N} + \text{C} \quad \text{O} \\
\text{H} \quad \text{O} \\
\text{C} \quad \text{C} \quad \text{O} \\
\text{CH}_2
\]

Tyrosine (Tyr or Y)

OH
Cysteine

\[ \text{H}_3\text{N} + \text{C} = \text{C} - \text{O} \]

\[ \text{CH}_2\text{SH} \]

Cysteine

\((\text{Cys or C})\)
Lysine

\[ \text{H}_3\text{N}-\text{C}\overset{\text{H}}{\text{C}}\overset{\text{C}}{\text{C}}\overset{\text{O}}{\text{O}}\overset{+}{\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_3}^{-} \]
Arginine

(Arg or R)

Arginine

+ 

NH₂

H₃N⁺

CH₂CH₂CH₂NH₂CNH₂
Histidine

\[
\begin{align*}
\text{H}_3\text{N} & \quad \text{C} \quad \text{C} \quad \text{O} \\
\text{H} & \quad \text{O} \\
\text{CH}_2 &
\end{align*}
\]

\text{Histidine} \quad \text{(His or H)}
Posttranslational modification of Amino Acids

Proline

Hydroxyproline

Lysine

Hydroxylysine

Tyrosine

Thyroxine
Titration of amino acids: what happens?
And what is an isoelectric point (pI)?

\[ pI = \frac{pK_{a1} + pK_{a2}}{2} \]

\[ \text{Cationic form} \quad \text{Neutral} \quad \text{Anionic form} \]

\[ \text{H}_3\text{N}^+ \quad \text{H}_3\text{N}^- \quad \text{H}_2\text{N}^- \quad \text{H}_3\text{N}^+ \quad \text{H}_3\text{N}^- \]

\[ \text{pK}_a = 2.34 \quad \text{pK}_a = 9.69 \]

\[ \text{pK}_1 = 2.34 \quad \text{pK}_2 = 9.69 \]

\[ \text{H}_2\text{NCHRRCOO}^- \quad \text{H}_3\text{NCHRCOO}^- \]

\[ \text{H}_2\text{NCHRRCOO}^- \quad \text{H}_3\text{NCHRCOO}^- \]

\[ \text{Moles of OH}^- \text{ per mole of amino acid} \]

\[ \text{pH} \]

\[ \text{Moles of OH}^- \text{ per mole of amino acid} \]
General rules for amino acid ionization

- Alpha carboxylic acids ionize at acidic pH & have pKs < 6; So in titration, alpha carboxylic acids lose the proton first
- Alpha amino groups ionize at basic pH & have pKs > 8; So after acids lose their protons, amino groups lose their proton
- Most of the 20 amino acids are similar to Gly
- There are 5 exceptions (Glu, Asp, Lys, Arg, His)
- Each has 3 ionizable groups and thus, 3 pKs
- Carboxylic acid groups near an amino group in a molecule have a more acidic pK than isolated carboxylic groups
- Amino groups near a carboxylic acid group also have a more acidic pK than isolated amines
General rules for amino acid ionization

- Aromatic amines like His have a pK about pH 6
- On titration: alpha carboxylic acids lose their proton first, then side chain carboxylic acids, then aromatic amine side chains (His), then alpha amino groups, then side chain amino groups
- These rules apply to small peptides too
The peptide bond, peptides, and proteins
Amino Acids & life
Amino acids & life

• Two amino acids deserve special attention (**Tyr & Trp**) with respect to neurotransmission

• Tryptophan converted to 5-hydroxytryptamine (**serotonin**, sedative effect)

• Very low levels are associated with depression, while extremely high levels produce manic state

• Tryptophan, milk & sleep
Amino acids & life

- The active products of Tyr metabolism are monoamine derivatives (MA). MAOs
- Headaches and Phe in aspartame
- Phe, Tyr, catecholamines; epinephrine (adrenalin). MAOᵢ makes metabolism slow
- *A Beautiful Mind, focused on Dopamine*
- Tyrosine supplements & morning lift
- Cheese and red wines (tyramine; mimics epinephrine); a cheese omelet is a favorite way to start the day
Other amino acids

- **Glutamic Acid**: Monosodium glutamate, or MSG, a flavor enhancer. MSG causes a physiological reaction in some people, with chills, headaches, and dizziness resulting in (*Chinese restaurant syndrome*).

- **Histidine**: converted to histamine, a potent vasodilator, part of the immune response, results in swelling and stuffiness that are associated with cold. Most cold medications contain antihistamines to overcome this stuffiness.
Aspartame, the Sweet Peptide

- L-aspartyl-L-phenylalanine, commercial importance
- The methyl ester derivative is called aspartame
- 200 times sweeter than sugar
Phenylketonuria

- Inborn errors of metabolism; errors in enzymes of amino acids metabolism
- May have disastrous consequences (mental retardation)
- Phenylketonuria (PKU) is a well-known example
- PKU can be easily detected and managed in newborns
- Aspartame carry a warning
- Alatame (Ala instead of Phe) is a substituent
Small Peptides with Physiological Activity

- Carnosine (dipeptide), found in muscle tissue, (β-alanyl-L-histidine), anti-oxidant

- Glutathione (tripeptide; g-glutamyl-L-cysteinylglycine); a scavenger for oxidizing agents
Small Peptides with Physiological Activity

• Enkephalins (pentapeptides), naturally occurring analgesics
  Tyr—Gly—Gly—Phe—Leu (Leucine enkephalin)
  Tyr—Gly—Gly—Phe—Met (Methionine enkephalin)

• Similarities of three-dimensional structures to opiates (e.g., morphine)

• Some important peptides have cyclic structures. Two well-known examples, oxytocin and vasopressin
Vasopressin stimulates reabsorption of water by the kidney, thus having an antidiuretic effect.