

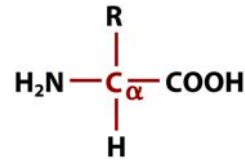
Amino Acids

(9/08/2009)

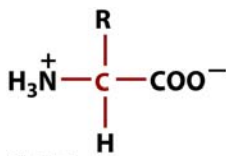
1. What are Amino Acids, and what is their 3-D structure?
2. What are the structures & properties of the individual amino acids?
3. What is the peptide bond?
4. Do amino acids have specific Acid-Base properties?
5. Are small peptides physiologically active?

Amino Acids

The building blocks of proteins



α-amino acids because of an amino group next to the C_α
R group - determines the identity of the particular amino acid
Stereochemistry - important property



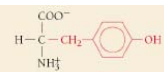
Amino acids are Amphotytes

$pK_1 \approx 2.2$ while $pK_2 \approx 9.4$, pK_R for R group pK 's
In the physiological pH range, both NH₂ and COOH are completely ionized
 They can act as either an acid or a base
 They are **Zwitterions**, molecules having charged groups of opposite polarity
 Because of their ionic nature they have extremely high melting temperatures

Amino Acids

You must know:

- Their names
- Their structure
- Their three letter code
- Their one letter code



Tyrosine, Tyr, Y, aromatic, hydroxyl

Classification and Characteristics of Amino Acids

R polarity: three main categories to describe amino acids:

- 1) **Non polar "hydrophobic" nine in all**
 Glycine, Alanine, Valine, Leucine, Isoleucine, Methionine, Proline, Phenylalanine and Tryptophan
- 2) **Uncharged polar, six in all**
 Serine, Threonine, Asparagine, Glutamine, Tyrosine, Cysteine
- 3) **Charged polar, five in all**
 Lysine, Arginine, Glutamic acid, Aspartic acid, and Histidine

Key to structure

(1)

	Name, Three-letter Symbol, and One-letter Symbol	Structural Formula ^a	Residue Mass (Da) ^b	Average Occurrence in Proteins (%) ^c	pK _a α-COOPH ^d	pK _a α-NH ₃ ⁺	pI _{iso} , Side Chain ^e
Amino acids with nonpolar side chains							
G	Glycine	COO ⁻	75.0	7.2	2.35	9.70	
	Gly	H-C-H					
A	Alanine	COO ⁻	89.1	7.8	2.35	9.67	
	Ala	H-C-CH ₃					
V	Valine	COO ⁻ CH ₃	99.1	6.6	2.29	9.74	
	Val	H-C-CH(CH ₃) ₂					
L	Leucine	COO ⁻ (CH ₃) ₂	133.2	9.1	2.33	9.74	
	Leu	H-C-CH ₂ -CH(CH ₃) ₂					
I	Isoleucine	COO ⁻ (CH ₃) ₂	133.2	5.3	2.32	9.76	
	Ile	H-C-CH(CH ₃)-CH ₂ -CH ₃					
M	Methionine	COO ⁻	149.2	2.3	2.13	9.29	
	Met	H-C-CH ₂ -CH ₂ -S-CH ₃					
P	Proline	H ₂	97.1	3.2	1.95	10.04	
	Pro	COO ⁻ CH ₂					
F	Phenylalanine	COO ⁻	147.2	3.9	2.20	9.31	
	Phe	H-C-CH ₂ -C ₆ H ₅					
W	Tryptophan	COO ⁻	204.2	1.4	2.46	9.41	
	Try	H-C-CH ₂ -C ₈ H ₆ N ₂					

(2)

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula ^a	Residue Mass (Da) ^b	Average Occurrence in Proteins (%) ^c	pK _a α-COOH ^d	pK _a α-NH ₃ ⁺ ^e	pK _a Side Chain ^f
Amino acids with uncharged polar side chains						
Serine Ser S		87.1	6.8	2.19	9.21	
Threonine Thr T		101.1	5.9	2.09	9.10	
Asparagine ^g Asn N		114.1	4.3	7.14	8.77	
Glutamine ^g Gln Q		126.1	4.3	2.17	9.13	
Tyrosine Tyr Y		180.2	3.2	2.20	9.21	10.46 (phenol)
Cysteine Cys C		103.1	1.9	1.92	10.70	8.37 (sulfhydryl)

Cystine consists of two disulfide-linked cysteine residues

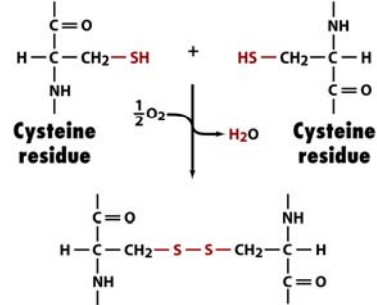
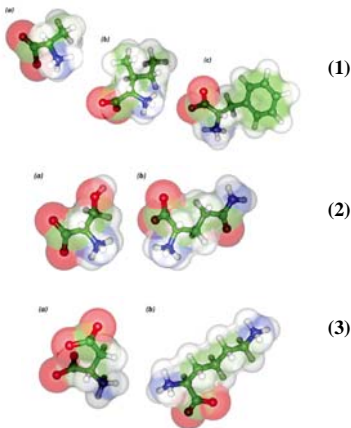
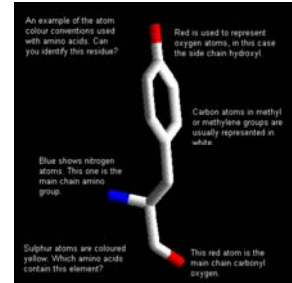


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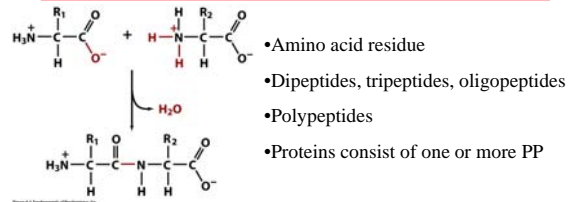
(3)

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula ^a	Residue Mass (Da) ^b	Average Occurrence in Proteins (%) ^c	pK _a α-COOH ^d	pK _a α-NH ₃ ⁺ ^e	pK _a Side Chain ^f
Amino acids with charged polar side chains						
K Lysine Lys K		128.2	5.8	2.16	9.06	10.54 (α-NH ₂)
R Arginine Arg R		196.2	5.1	1.82	8.99	12.48 (guanidino)
H Histidine His H		133.1	2.3	1.80	8.13	6.04 (imidazole)
D Aspartic acid Asp D		113.1	5.3	1.99	9.90	3.90 (β-COOH)
E Glutamic acid Glu E		129.1	6.2	2.10	9.47	4.07 (γ-COOH)

Color conventions



Amino acids can form peptide bonds CO-NH linkage



Peptides are linear polymers that range from 8 to 4000 amino acid residues

Twenty (20) different naturally occurring amino acids

Linear arrays of amino acids can make a huge number of molecules

Consider a peptide with two amino acids



$$20 \times 20 = 400 \text{ different molecules}$$



$$20 \times 20 \times 20 = 8000 \text{ different molecules}$$

For 100 amino acid protein the # of possibilities are:

$$20^{100} = 1.27 \times 10^{130}$$

The total number of atoms in the universe is estimated at 9×10^{78}

Acid - Base properties of amino acids

$$\text{pH} = \text{pK} + \log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right)$$

Isoelectric point: the pH where a protein carries no net electrical charge

$$\text{pI} = \frac{1}{2}(\text{pK}_i + \text{pK}_j)$$

For a monoamino-monocarboxylic residue

$$\text{pK}_i = \text{pK}_1 \text{ and } \text{pK}_j = \text{pK}_2;$$

For D and E, $\text{pK}_i = \text{pK}_1$ and $\text{pK}_j = \text{pK}_R$;

For R, H and K, $\text{pK}_i = \text{pK}_R$ and $\text{pK}_j = \text{pK}_2$

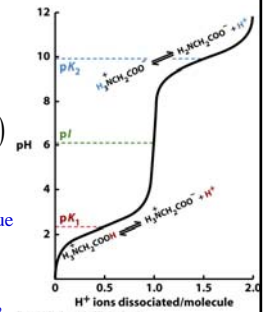
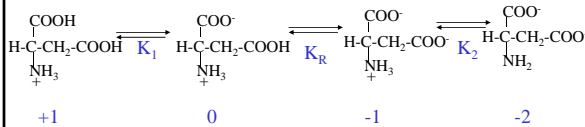
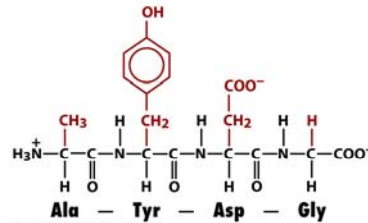


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Tripeptide	Molecular Weight	Structural Formula	Residue	Average Molecular Weight	pI	pKa	pKa
Alanine	89.09	<chem>CC(N)C(=O)O</chem>	Alanine	89.09	9.69	2.34	9.69
Aspartic acid	133.07	<chem>CC(N)C(=O)OCC(=O)O</chem>	Aspartic acid	133.07	2.97	3.90	9.59
Glutamic acid	146.07	<chem>CC(N)C(=O)OCCC(=O)O</chem>	Glutamic acid	146.07	3.22	4.25	9.47
Lysine	146.15	<chem>CC(N)C(=O)OCCCCN</chem>	Lysine	146.15	9.74	10.49	10.49



Nomenclature

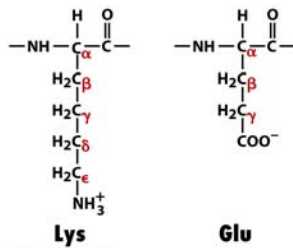


The tetrapeptide Ala-Tyr-Asp-Gly or AYDG

Greek alphabet

Beginner's guide to the Greek alphabet.

- α alpha
- β beta
- γ gamma
- δ delta
- ε epsilon
- ζ zeta
- η eta
- θ theta
- φ phi
- χ chi
- ψ psi
- ω omega



Greek lettering used to identify atoms in lysine or glutamate

Stereochemistry

Optical activity - The ability to rotate plane - polarized light

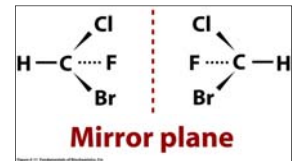
Asymmetric carbon atom

Chirality - Not superimposable

Mirror image - enantiomers

(+) Dextrorotatory - right - clockwise

(-) Levorotatory - left counterclockwise



Operational definition only

Cannot predict absolute configurations

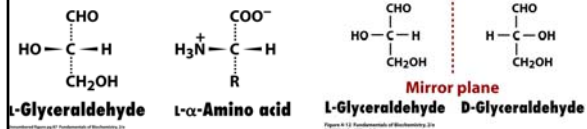
The Fischer Convention

Absolute configuration about an asymmetric carbon

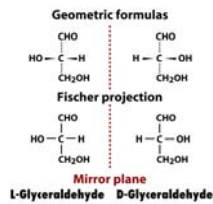
related to glyceraldehyde

(+) = D-Glyceraldehyde

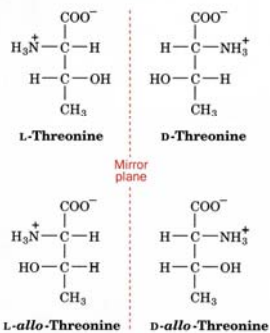
(-) = L-Glyceraldehyde



All naturally occurring amino acids that make up proteins are in the L conformation



An example of an amino acid with two asymmetric carbons

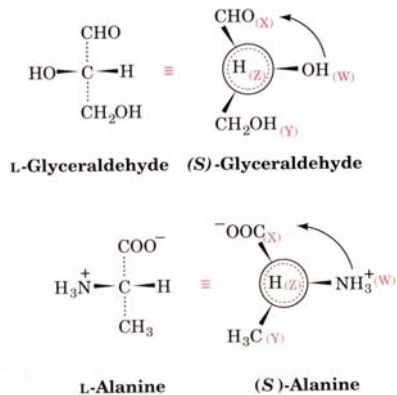


Cahn - Ingold - Prelog system

Can give absolute configuration nomenclature to multiple chiral centers.

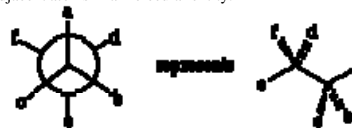
Priority

Atoms of higher atomic number bonded to a chiral center are ranked above those of lower atomic number with lowest priority **away from you** R highest to lowest = clockwise, **S** highest to lowest = counterclockwise



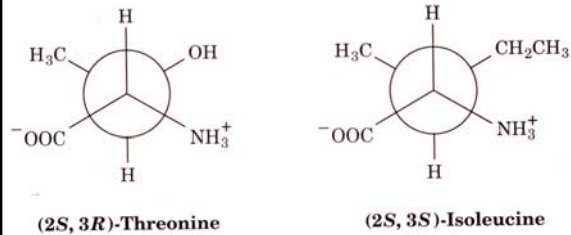
Newman Projection

- A *projection formula* representing the spatial arrangement of bonds on two adjacent atoms in a molecular entity.



- The structure appears as viewed along the bond between these two atoms, and the bonds from them to other groups are drawn as projections in the plane of the paper.
- The bonds from the atom nearer to the observer are drawn so as to meet at the centre of a circle representing that atom.
- Those from the further atom are drawn as if projecting from behind the circle.

The major advantage of the CIP or RS system is that the chiralities of compounds with multiple asymmetric centers can be unambiguously described



Side Chain Modifications in Proteins

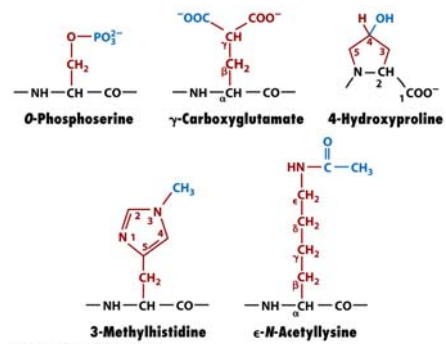


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Biologically Active Amino Acids

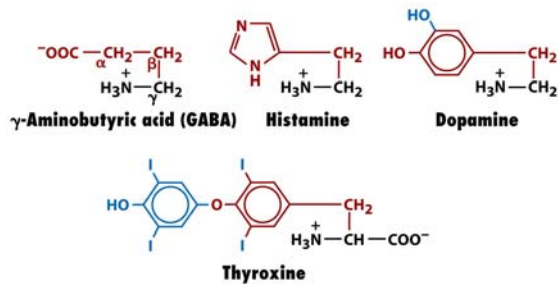
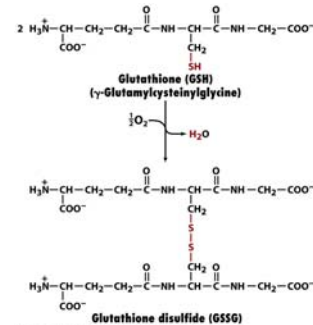


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Oxidation and Reduction of Glutathione



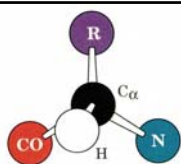
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Questions:

- For the dipeptide Tyr-Asp, find pI (the pK s are α -amino 9.2, phenolic 10.5, β -carboxylate 3.9, α -carboxylate 2.0).
- For the dipeptide Lys-Glu, find pI (the pK s are α -amino 9.1, ϵ -amino 10.5, γ -carboxylate 4.1, α -carboxylate 2.1).

Lecture 6
Thursday 9/10/09
Amino Acids

The CORN method for L isomers:
 put the hydrogen towards you and
 read off CO R N clockwise
 around the C_{α} . This works for all
 amino acids.



CORN LAW amino acid with L configuration

