Amino Acids

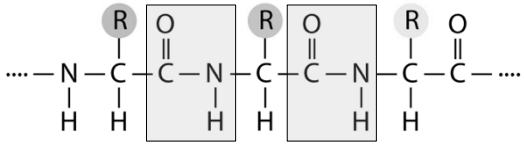
Proteins: *Structure & Function*

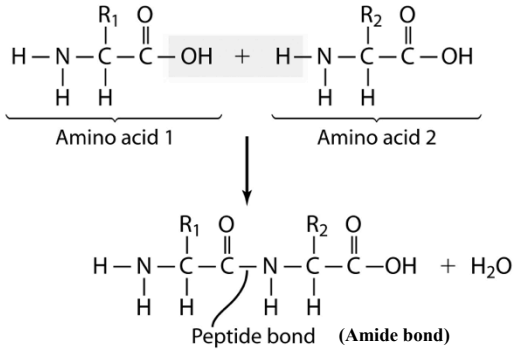
Proteins

Polypeptides, Amides and Proteins

- **Proteins are polyamides, each amide group is called a peptide bond.**
- **Peptides are formed by condensation of the -COOH group of one amino acid and the NH group of another amino acid.**

Amides & Proteins





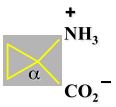
Proteins

- **Polypeptides and Proteins**
- **The acid forming the peptide bond is named first. Example: if a dipeptide is formed from alanine and glycine so that the COOH group of glycine reacts with the NH group of alanine, then the dipeptide is called glycylalanine.**

Fundamentals

- **While their name implies that amino acids are compounds that contain an —NH_2 group and a —CO_2H group, these groups are actually present as —NH_3^+ and —CO_2^- respectively.**
- **They are classified as α, β, γ, *etc*. amino acids according the carbon that bears the nitrogen.**

Amino Acids



an α-amino acid that is an intermediate in the biosynthesis of ethylene

$^{+}H_3NCH_2CH_2CO_2^{-}$ (β α)

a β-amino acid that is one of the structural units present in coenzyme A

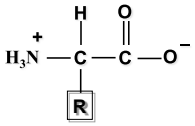
$^{+}H_3NCH_2CH_2CH_2CO_2^{-}$ (γ β α)

a γ-amino acid involved in the transmission of nerve impulses

The 20 (22) Key Amino Acids

- **More than 700 amino acids occur naturally, but 20 (22?)of them are especially important.**
- **These 22 amino acids are the building blocks of proteins. All are α-amino acids.**
- **They differ in respect to the group attached to the α carbon.**

Amino Acids

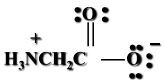


- **The amino acids obtained by hydrolysis of proteins differ in respect to R (the side chain).**
- **The properties of the amino acid vary as the structure of R varies.**

Properties of Glycine

- **The properties of glycine:**
  - **high melting point (when heated to 233°C it decomposes before it melts)**
    solubility: soluble in water; not soluble in nonpolar solvent

more consistent with this



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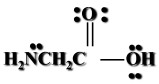

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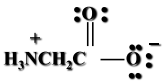

called a *zwitterion* or *dipolar ion*

Acid-Base Properties of Glycine

- **The zwitterionic structure of glycine also follows from considering its acid-base properties.**
- **A good way to think about this is to start with the structure of glycine in strongly acidic solution, say pH = 1.**
- **At pH = 1, glycine exists in its protonated form (a monocation).**

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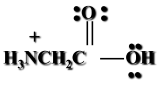
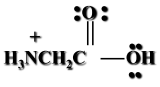


Acid-Base Properties of Glycine

- Now ask yourself "As the pH is raised, which is the first proton to be removed? Is it the proton attached to the positively charged nitrogen, or is it the proton of the carboxyl group?"
- You can choose between them by estimating their respective pK_as.



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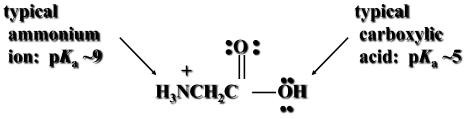
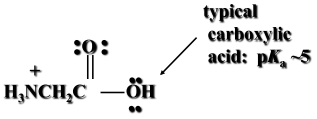


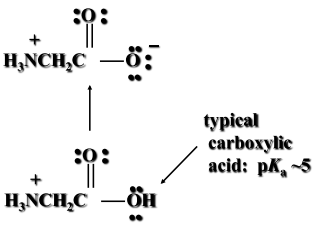
Acid-Base Properties of Glycine

- The more acidic proton belongs to the CO_2H group. It is the first one removed as the pH is raised.



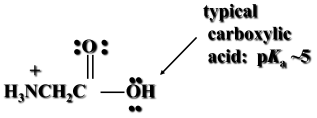
Acid-Base Properties of Glycine

- Therefore, the more stable neutral form of glycine is the zwitterion.



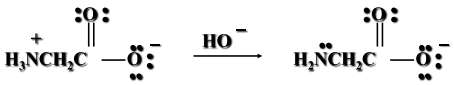
Acid-Base Properties of Glycine

- The measured pK_a of glycine is 2.34.
- Glycine is stronger than a typical carboxylic acid because the positively charged N acts as an electron-withdrawing, acid-strengthening substituent on the α carbon.



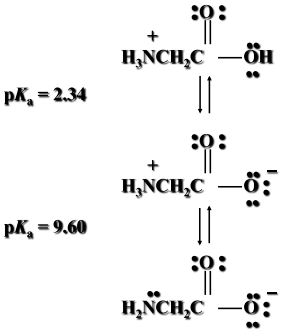
Acid-Base Properties of Glycine

A proton attached to N in the zwitterionic form of nitrogen can be removed as the pH is increased further.



- The pK_a for removal of this proton is 9.60. This value is about the same as that for NH_4^+

Isoelectric Point pI



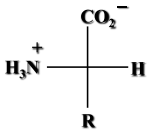
- The pH at which the concentration of the zwitterion is a maximum is called the *isoelectric point*. Its numerical value is the average of the two pK_as.
- The p*I* of glycine is 5.97.

Acid-Base Properties of Amino Acids

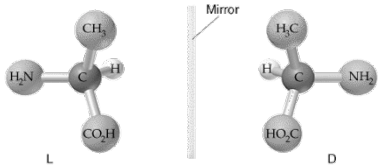
- One way in which amino acids differ is in respect to their acid-base properties. This is the basis for certain experimental methods for separating and identifying them.
- Just as important, the difference in acid-base properties among various side chains affects the properties of the proteins that contain them.

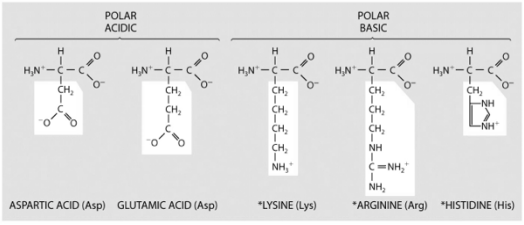
Configuration of α-Amino Acids

- Glycine is achiral. All of the other amino acids in proteins have the L-configuration at their α carbon.



Amino Acids



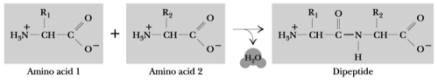


Amino Acids

Amino Acids:

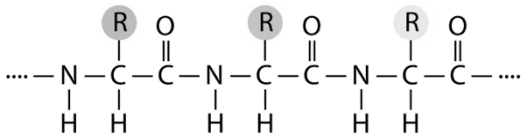
Name	3	1	R-	R'	Reacted Color	Function & Class
Alanine	Ala	A	H-	CH_3	dark gray	Aliphatic Hydrophobic
Arginine	Arg	R	H-	$(CH_2)_3NHC(NH_2)NH_2$	blue	Basic Hydrophilic
Asparagine	Asn	N	H-	CH_2CONH_2	cyan	Amide Highly Hydrophilic
Aspartate	Asp	D	H-	CH_2COH	bright red	Acidic Hydrophilic
Cysteine	Cys	C	H-	CH_2SH	yellow	Sulphur Containing Hydrophobic
Glutamine	Gln	Q	H-	$CH_2CH_2CONH_2$	cyan	Amide Highly Hydrophilic
Glutamate	Glu	E	H-	CH_2CH_2COH	bright red	Acidic Hydrophilic
Glycine	Gly	G	H-	H-	light gray	Aliphatic Hydrophobic
Histidine	His	H	H-		pale blue	Basic Hydrophilic
Isoleucine	Ile	I	H-	$CH_3CHCH_2CH_3$	green	Aliphatic Hydrophobic
Leucine	Leu	L	H-	$CH_2CHCH_3CH_3$	green	Aliphatic Hydrophobic
Lysine	Lys	K	H-	$(CH_2)_4NH_2$	blue	Basic Hydrophilic
Methionine	Met	M	H-	$CH_2CH_2SCH_3$	yellow	Sulphur Containing Hydrophobic
Phenyl-alanine	Phe	F	H-		mid blue	Aromatic Hydrophobic
Proline	Pro	P	-		flesh	Aliphatic Hydrophobic
Serine	Ser	S	H-	CH_2OH	orange	Hydroxylic Hydrophobic
Threonine	Thr	T	H-	$CHOHCH_3$	orange	Hydroxylic Hydrophobic
Tryptophan	Trp	W	H-		pink	Aromatic Hydrophobic
Tyrosine	Tyr	Y	H-		mid blue	Aromatic Hydrophobic
Valine	Val	V	H-	CH_3CHCH_3	green	Aliphatic Hydrophobic

Polymers of Amino Acids



Amino acid 1 Amino acid 2 Dipeptide

- **Peptides have various numbers of amino acids.**
- **Peptides are always written with the -NH_2 terminus on the left, -CO_2H on the right.**
- **Each amino acid unit is called a residue.**
- **2 residues = dipeptide,**
- **3 residues = tripeptide,**
- **12-20 residues = oligopeptide,**
- **Many residues = polypeptide.**



Proteins, Peptides & Structure

Proteins (Polypeptides)

Polypeptides

- **Polypeptides are formed with a large number of amino acids (usually result in proteins with molecular weights between 6000 and 50 million amu).**

Protein Structure

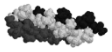
- **Primary structure is the sequence of the amino acids in the protein.**
- **A change in one amino acid can alter the biochemical behavior of the protein. *Eg. Sickle Cell Anemia***

Proteins

- **Polypeptides and Proteins**
- **Glycylalanine is abbreviated gly-ala or GA.**
- **Polypeptides are formed with a large number of amino acids (usually result in proteins with molecular weights between 6000 and 50 million amu).**
- **Protein Structure**
- **Primary structure is the sequence of the amino acids in the protein.**
- **A change in one amino acid can alter the biochemical behavior of the protein.**

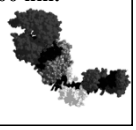
Examples of Protein Types -

- **Enzymes: *Glutamine synthetase* - 12 subunits of 468 residues each; total mol. wt. = 600,000 daltons**
- **Regulatory proteins: *Insulin* - α -alpha chain of 21 residues, β - beta chain of 30 residues; total mol. wt. of 5,733 amu**



- **Structural proteins: *Collagen***

  ***Connectin proteins*, β - MW of 2.1 million g/mol; length = 1000 nm; can stretch to 3000 nm.**
- **Transport proteins: *Hemoglobin***



- **Contractile proteins: *Actin, Myosin***
- **Specialized proteins: *Antifreeze in fish***

Four Levels of Protein Structure

- **1º : The linear sequence of amino acids and disulfide bonds eg. ARDV:Ala-Arg-Asp-Val.**
- **2º : Local structures which include, folds, turns, ∝-helices and β -sheets held in place by hydrogen bonds.**
- **3º : *3-D* arrangement of all atoms in a single polypeptide chain.**
- **4º : Arrangement of polypeptide chains into a functional protein, eg. hemoglobin.**

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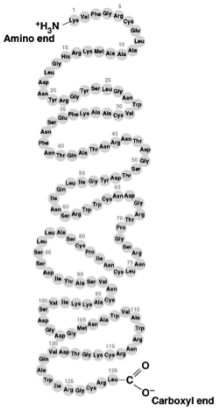
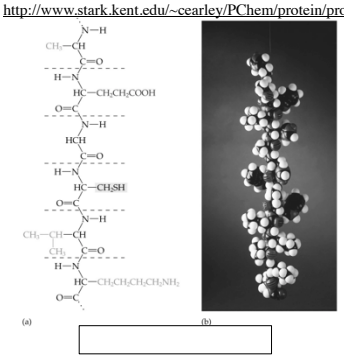
- **The primary structure of a protein is its unique sequence of amino acids.**
  - **Lysozyme, an enzyme that attacks bacteria, consists on a polypeptide chain of 129 amino acids.**
  - **The precise primary structure of a protein is determined by inherited genetic information.**

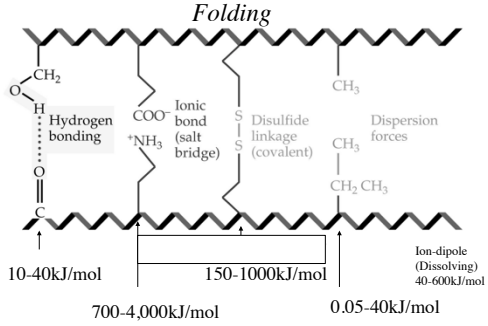


Proteins: Size, Shape & Self Assembly

http://www.stark.kent.edu/~cearley/PChem/protein/protein.htm



Protein Shape: Forces, Bonds, Self Assembly, Folding



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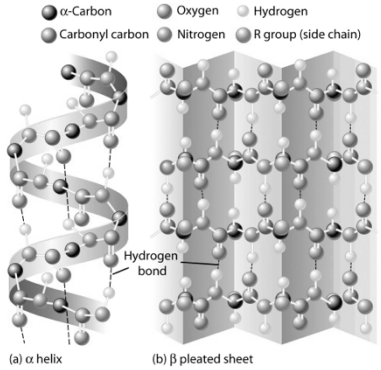
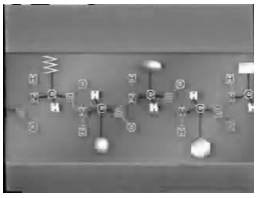


Hair: α-Helix



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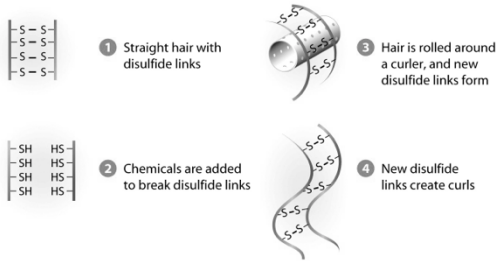
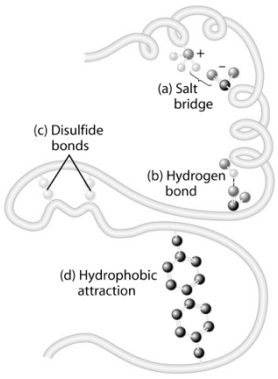
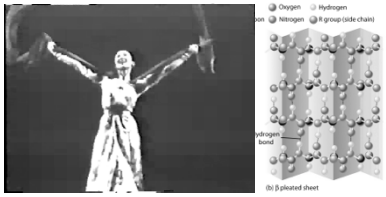




Silk: β-Sheets



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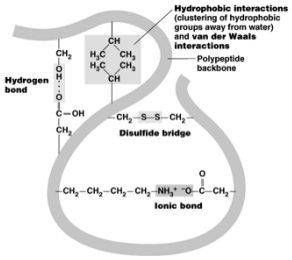
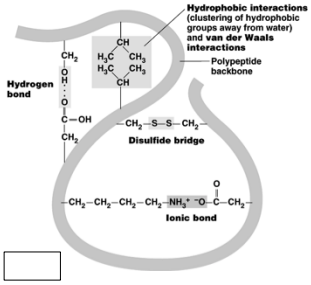
- Tertiary structure **is determined by a variety of interactions among R groups and between R groups and the polypeptide backbone.**



- **While these three interactions are relatively weak,** disulfide bridges**, strong covalent bonds that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.**



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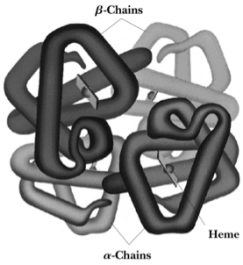
The quaternary structure of hemoglobin, Hb

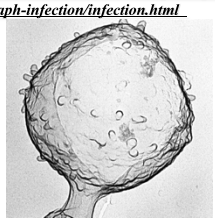
(A tetramer)

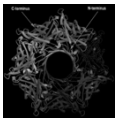


Hb: two alpha units of 141 residues, 2 beta units of 146

Mechanical proteins
Pathogens & Cell Invasion

http://chemconnections.llnl.gov/organic/chem226/Announcements-info/Staph-infection/infection.html





Streptococcus pyogenes
96,000 x
Vincent A. Fischetti Ph.D., Rockefeller University